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TUBERCULOSIS CONTROL IN DENMARK

By E. GROTH-PETERSEN

Tuberculosis mortality is declining rapidly in most countries of the world, including Denmark, which for many years now has been among the nations with the lowest tuberculosis mortality on record; in 1954 it was 7.7 per 100,000 population, tuberculosis of all forms claiming a total of 341 deaths in our population of 4.4 million.

Tuberculosis morbidity, on the other hand, is decreasing less rapidly. In many countries it seems to have remained constant since the war, whereas in some it has even increased. The mortality figures alone therefore give only an incomplete picture of the tuberculosis situation, and since the object is to prevent tuberculosis, there is a growing interest in international comparisons of the prophylactic work and its results.

Statistics on tuberculosis morbidity are, however, difficult to compare. Their completeness varies markedly from country to country, depending on the extent of tuberculosis control and the efficiency of the notification system.

To provide a background for subsequent morbidity studies, we shall give a brief account of tuberculosis control in Denmark (excluding Greenland and the Faroe Islands) with comments on such features of its philosophy, history and legislative basis as are of importance to its present organization as well as some data on the scope of the case-finding and vaccination activities and on the results obtained.

More detailed information on the period up through 1949 may be found in "The Fight against Tuberculosis in Denmark" issued by the *National Association for the Fight against Tuberculosis* (Copenhagen, 1950).

From the Danish Tuberculosis Index.
Chief: *E. Groth-Petersen.*
The Danish Tuberculosis Index is a co-operative research enterprise established in 1950 by the National Health Service of Denmark, Director-General *Johs. Frandsen,* M. D., and the World Health Organization Tuberculosis Research Office, Director *Carroll E. Palmer,* M. D., Ph. D.

THE PHILOSOPHY

Tuberculosis is prevented by preventing the spread of infection and by increasing the resistance against infection, and these two aspects of the problem are inseparable in the fight against tuberculosis in man. Ever since the discovery of the tubercle bacillus, the greatest importance in direct prophylactic work has been attached to the prevention of the spread of infection, but the immense improvement in living conditions in the present century has no doubt mainly led to an increase in resistance. As late as the beginning of the 'thirties almost the entire Danish population was tuberculosis-infected before attaining the age of 40 years, but the tuberculosis mortality of the nation was nevertheless the lowest in Europe.

In the prevention of infection the most important factor is early recognition of all cases of the disease, but if early recognition leads to unemployment, poverty and want, weakening the resistance of the patient and his dependents, "early diagnosis" becomes a double-edged sword that may do more harm than good. The value of modern intensive case-finding therefore depends on to what extent the patients are secured rapid access to treatment, to what extent social and hygienic protection are secured for the patient and his family during and after treatment, and whether or not a decent future awaits the patient whom treatment fails to cure.

HISTORICAL DEVELOPMENT

The establishment of sanatoria and hospitals.

In Danish anti-tuberculosis work the chief emphasis was for many years placed upon the establishment of treatment centres, at first for ex-

trapulmonary tuberculosis: the Seaside Hospital at Refsnæs in 1875 (Sophus Engelsted), the Finsen Institute in 1895 (Niels Finsen); and later for pulmonary tuberculosis: Vejlefjord Sanatorium in 1900 (Saugman) and Boserup Sanatorium in 1901 (municipality of Copenhagen). Today Vejlefjord Sanatorium is our only private sanatorium for paying patients. The National Association for the Fight against Tuberculosis (NA) was founded in 1901 and established in the following years in different parts of the country the present nine sanatoria for patients with pulmonary tuberculosis, one hospital for extrapulmonary tuberculosis, some nursing and convalescent homes as well as a number of preventoria. The NA — unlike similar associations in most other countries — still owns and runs these sanatoria, but the State defrays practically all the working expenses, and the management of the sanatoria is therefore subject to government control. This arrangement also applies to Krabbesholm Sanatorium, which is owned and managed by the Danish Agricultural Co-operative Societies. At the beginning of this century, moreover, many communes established small tuberculosis hospitals in connection with the local general hospitals, with the result that already in 1920 the number of tuberculosis beds exceeded the annual number of deaths from tuberculosis.

Right up to the mid-thirties the treatment of the tuberculous held a dominant position in the fight against tuberculosis in Denmark. The results of treatment were, however, as everywhere else, rather meagre. Furthermore, at that time, the sanatoria followed a most unfortunate practice of not admitting patients who were too ill to be up; such patients could gain admittance only to the tuberculosis hospitals, which only as an exceptionally were under the direction of a tuberculosis specialist. Thus a sharp line was drawn between patients with moderate and those with advanced disease, which made it difficult to effect hospitalization for purposes of nursing and isolation. Though the leading physicians of the sanatorium movement themselves regarded the prevention of infection as the most effective factor in the long run, it was only during the later developed chest clinic system that this unfortunate differentiation was abolished.

The development of the chest clinic.

According to the ideas of Robert Philip (8) (The Victoria Dispensary, Edinburgh 1887), the tuberculosis dispensaries should function as real centres for the prevention and diagnosis as well as the treatment of the disease. Dispensaries of this type were established late in Denmark, but from 1908 the NA opened small dispensaries (in Danish: Tuberkulosestation) in Copenhagen and later also in several other towns, the main function of which was to assist the general practitioners in the supervision of the tuberculous patients and their families and to help to improve the hygienic and economic conditions in the patients' homes. When Johs. Frandsen became Chief of the National Health Service in 1928, he strongly promoted a thorough reorganization of the preventive and diagnostic work involving the successive establishment in each county of "chest clinics" run by the local authorities and attached to central hospitals with specialized departments. This gradually led to the organization of tuberculosis control as it exists today (page 163). Tuberculosis control in Copenhagen was reorganized in 1935 (Knud Winge), but it was not until 1945 that the whole country was covered by "chest clinics", which term will be used for the modern tuberculosis dispensary which is a centre for the tuberculosis control work and to a large extent also a diagnostic centre for chest diseases. (Fig. 1).

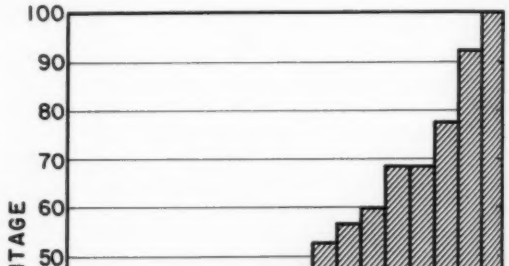

Fig. 1.
Percentage of population served by chest clinics, Denmark outside Copenhagen, 1929—46.

Tuberculosis in cattle.

An early aim of the direct phophylactic work was the eradication of tuberculosis in cattle, which was highly prevalent in Denmark in the eighties. The first measures were adopted as early as 1892, when Bernhard Bang presented his plan for a rational fight against tuberculosis in cattle through systematic prevention of infection, but it was not until 1932 that the work assumed important proportions and only in 1952 was the goal attained (see N. Plum, p. 169 in this issue of the Danish Medical Bulletin).

Legislation, provisions applying to subsidies and public assistance.

Two Tuberculosis Acts of fundamental importance were enacted in 1905. These Acts embodied

provisions on welfare, such provisions being considered for the first time a necessary part of strict health laws. It should also be mentioned that this legislation introduced State support for the building of tuberculosis sanatoria and hospitals and for the treatment of patients in such institutions, that it granted toeachers, civil servants and other officials, dimissed on account of infectious tuberculosis, a pension amounting to two-thirds of their salary, and that it introduced compulsory medical notification of tuberculosis of the lungs and larynx. The excellent principles of these laws are still valid, although the laws have, of course, been brought up to date and improved over the years. In 1912 state subsidies for the tuberculosis dispensaries of the NA were granted by law, and in 1919 a paragraph was added — in force to this day — that provided that half of the working expenses of chest clinics run by the local authorities would be covered by the government. As mentioned before, no use was made of this provision until 1928.

Examination at the chest clinics is free of charge for all regardless of financial standing and insurance coverage. Treatment in tuberculosis hospitals and sanatoria is also free or nearly so, as the government and the local authorities in fact pay the treatment regardless of the patient's financial circumstances. Only a symbolic charge of D. kr. 1.50 per day, that is, about 5 per cent of the actual costs, is paid by the patient's sickness-benefit association or by the patient himself if he is prosperous and not insured.

The first legislation on public sickness-insurance was enacted in 1892, and about 80 per cent of the population are now insured through voluntary membership in the State-approved sickness-benefit associations and are thus entitled to free medical attention and free hospital or sanatorium treatment. All Danes are by law insured against disablement. Through this insurance they can obtain assistance for the prevention of disablement, for special treatment, vocational training, establishment in a new trade or business, etc. as well as a temporary or lifelong disablement pension.

The general public assistance legislation also applies to the tuberculous. To some extent this legislation has always favoured the tuberculous by personal supplements, though not sufficiently so in the earlier years to protect the patient and his family against an unfortunate reduction of their standard of living in case of protracted illness. Following a revision of the Public Assistance Act in 1949, however, the provisions on assistance for the tuberculous became satisfactory, almost ideal. Since then it has been possible to grant the tuberculous an assistance that covers more than just the minimum requirements of life, and patients who prior to their disease have lived in comfortable circumstances may be helped to maintain their previous standard of living for themselves and their families within reasonable limits. This really excellent assistance, however, can be granted only for four years, and it requires that the patient follow the directions of the chest clinic.

This assistance is of course intended to give the population such a feeling of security that fear of the social consequences of the disease will not prevent people from coming for examination and will not tempt patients who feel rather well and fit for work but are in need of treatment to refuse hospitalization or to resume work too early in the convalescent period.

The annual expenditure on assistance for the tuberculous represents a considerable part of the total State and local authority expenditure on anti-tuberculosis activities:

Expenditure on public assistance
approx. D. kr. 20,000,000
Expenditure on chest clinics
approx. D. kr. 7,000,000
Expenditure on hospitals & sanatoria
approx. D. kr. 30,000,000

To this must be added allowances made for better housing that often are paid from other accounts, and considerable grants from private funds, and from that of the National Association in particular, given to supplement public assistance.

PRESENT ORGANIZATION

Excluding the municipality of Copenhagen, Denmark is divided into 22 chest clinic areas, each with an average population of 160,000. In most cases the chest clinic area covers one county and contains a tuberculosis hospital (or department) and a central chest clinic attached to the central hospital of the county as well as 4 to 5 branch clinics attached to the general hospitals of the county. The tuberculosis hospital and the chest clinics are owned and run by the local authorities with a committee of members of the local (town or county) councils acting as supervisory board; and a chief chest physician, a qualified specialist, directs the work of both the tuberculosis hospital and the chest clinics without direct supervision by any higher, central authority. An essential feature of the system is that the chest clinics and the tuberculosis hospital have a joint medical staff. As a result of the historical development, some counties, however, operate a chest clinic but no tuberculosis hospital; these are counties where there already existed a State-approved sanatorium when the chest clinic was established and where the chest clinic therefore is attached to the sanatorium and shares its medical staff.

There is no medical distinction between the tuberculosis hospital and the sanatorium. All hospitals and sanatoria carry out hygienic-dietary treatment, chemotherapy, pneumothorax treat-

ment and adhesion operations, while the facilities for specialized surgical treatment are concentrated in a few large treatment centres in Copenhagen and Jutland.*) Rehabilitating treatment or other problems arising in the course of the disease may also require admission to another institution than the local tuberculosis department, and in principle it is essential that the patients are not confined to the local curative institutions but that all sanatoria admit patients from the whole country on equal terms, as mentioned previously.

The advantages and disadvantages of modern intensive case-finding depend, among other things, on the evaluation of the need for treatment. The conditions in the patient's home and the conditions under which he works must be taken into consideration when deciding whether treatment or observation only is required. We consider it a great advantage that the chest clinic physician is also the doctor in attendance, especially in the early stages of the disease when close contact with the patient is of such importance for the prophylactic work. Diagnostics, guidance, treatment and prophylaxis interlock to such an extent that co-ordination is necessary, and the problems are best solved under joint direction.

With the decreasing incidence of tuberculosis the practical difficulty arises that the number of tuberculosis patients and patients for observation admitted to hospital in the individual chest clinic areas becomes too small to justify the running of a local tuberculosis hospital. This problem can be solved by using the tuberculosis hospital to an increasing extent as a general chest disease unit or by an arrangement whereby several chest clinic areas together operate a tuberculosis hospital.

As mentioned, the municipality of Copenhagen forms a separate chest clinic unit with a population of about 760,000. Here it has unfortunately been necessary to divide the work among three tuberculosis specialists: the chief of the chest clinic, the chief of the tuberculosis hospital and the chief of the sanatorium. The chest clinic, however, directs the admission of patients both to the sanatorium and to the hospital, and the co-operation among the three institutions is as close as it can be without a joint medical staff.

The Armed Forces and the Copenhagen Prison Administration have their own chest clinics and observation wards.

The number of beds in curative institutions in the late 'thirties exceeded the annual number of new cases of pulmonary tuberculosis. In recent years it has been possible to reduce the number of beds, and at present we have 2500 beds for adults with respiratory tuberculosis and 340 beds for children, while the annual number of new cases only amounts to about 1500 adults and 200 children. The excess beds are temporarily being used for patients from Greenland and South Slesvig, and for English children.

The best possible facilities for treatment are thus at the disposal of the chest clinic service, and the same applies to facilities for relief through public assistance and private philanthropy. The latter is well organized, with the chest clinic serving as the connecting link between the patient and the various charitable institutions. It is of great value for the relief as well as the prophylactic work that all chest clinics have their own nurses for home visiting. Many chest clinics also have a specially trained social worker to help the patients with social and other problems.

As regards *rehabilitation*, our position is less favourable. True, progress has been made: occupational therapy is given during hospitalization, and since 1953 the NA has operated a factory in Copenhagen for the training and employment of tuberculous persons, and some of the provincial chest clinics too have taken measures to provide sheltered work — but these activities are on a limited scale and the difficulties are great. No doubt the best thing the chest clinics can do in this matter is to co-operate with the employment exchanges and to inform the authorities, the employers and the population about the detrimental effects of the exaggerated fear of the patients and the advantages of providing work for patients with chronic infectious tuberculosis under conditions ensuring maximum protection for their work contacts.

It is important that *the chest clinic is informed of all known cases* in its area. No doubt this has been ensured as well as it can be through our notification system and through co-operation with the State Serum Institute. As mentioned before, tuberculosis of the lungs has been a notifiable disease since 1905, and compulsory notification of all other forms of tuberculosis was introduced in 1951; furthermore, patients' changes of address are reported from clinic to clinic by way of the National Health Service.

The Tuberculosis Department of the State Serum Institute serves as a central laboratory for the entire country. All diagnostic examinations for tubercle bacilli, including those of specimens sent by general practitioners, are free of charge, and all positive findings are reported to the chest clinics. (Johs. Holm) (1).

CASE-FINDING

The most important factor in the prevention of infection is early recognition of all cases of the disease. X-ray examination of the chest has made early diagnosis possible, but it should be stressed that the diagnosis of tuberculosis can be confirmed only by the demonstration of tubercle bacilli. In this country great importance has al-

*) Concerning the principles of treatment may be referred to Hans Thomsen (10) and Kjeld Tørning (11).

ways been attached to the bacteriological examination, both in diagnosis and in therapy, and a diagnosis of pulmonary tuberculosis is made only reluctantly and rather infrequently if the presence of tubercle bacilli has not been demonstrated. Microscopic examination is done locally or at the Serum Institute. Examination by culture is performed only at the Serum Institute and is carried out whenever the microscopic examination is negative, or positive for the first time. In addition, cultures are always made of gastric washings, a diagnostic method that has steadily gained in importance since 1930.

Tuberculin testing with standardized tuberculin and technique is routinely performed on all persons.

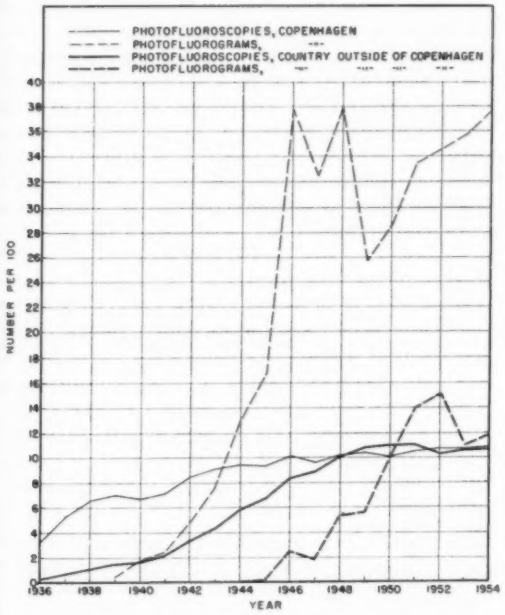

Fig. 2.
Number of photofluoroscopic and photofluorographic examinations per 100 population, Copenhagen and Denmark outside Copenhagen, 1936—54.

In general, fluoroscopy constitutes the standard method of x-ray examination in the daily work of the chest clinics. On the least suspicion of abnormal findings the fluoroscopic examination is followed up by full-size roentgenograms and, if necessary, by tomography and bronchoscopy. In some chest clinics, fluoroscopy is routinely supplemented by photofluorography, particularly when a person is examined for the first time. And for mass x-ray surveys only photofluorographic units — static or mobile — are used nowadays. Independent dual reading of the photofluorograms was introduced in 1950 and has led to a considerable increase in the case-finding rate in mass surveys.

Number of persons examined.

Information on the number of persons examined by the chest clinics is only partly available for the years prior to 1954. Judging, however, from the figures available and the number of x-ray examinations, etc., the extent of the examination work in Copenhagen markedly increased up to 1946 and has fluctuated around an annual total of 250,000 persons since that date; in the provinces the volume of examination increased up to 1951 and is estimated to have fluctuated around 500,000 thereafter.

Not until 1954 tabulations of the number of persons examined were made in all chest clinic areas, and in addition the reason for the first examination in the year was recorded for all adults (15 years and over). In all, 220,000 children — excluding those examined for tuberculosis by the School Health Officers only — and 833,000 adults were examined. Of the latter, 18,000 were examined because of a previously diagnosed tuberculosis. *Out of a total adult population of 3.2 millions, 815,000 or 25 per cent have thus been examined by the chest clinics as part of their case-finding work in 1954.* The percentage of adults examined, however, is markedly different for rural and urban populations and for males and females. (Table 1).

Table 1.
Percentage of Adult Population Examined by the Chest Clinics in 1954, by Sex and Main Provinces.

	Men	Women	Total Population
Copenhagen and Copenhagen county ..	46	30	37
Provincial towns	39	26	32
Rural districts	14	10	12
Entire country	30	21	25

Information on the examination rates for individual districts of residence is only approximate, as some of the persons participating in group examinations are not tabulated by place of residence but by place of work alone. It appears from the official statistics on the distribution of the population by borough of residence and borough of occupation and those on the number of non-residents paying taxes to the borough of occupation that a large part of the population of Greater Copenhagen lives in one borough and works in another, the majority living in the outlying boroughs and working in the central boroughs. Copenhagen city and Copenhagen county must therefore be treated as one unit. In the rest of Denmark there appears to be much less "commuting" from country to town and, besides, so few of the adults examined have been tabulated by place of work that "commuting" will not affect the examination rates.

Outside Greater Copenhagen examination rates by sex can be given for only three-fourths of the population.

The adults examined may be divided into three groups according to the reason for attendance:

A. Examination occasioned by symptoms.

Time and again experience has shown that tuberculosis infection is mainly propagated by persons with undiagnosed pulmonary tuberculosis who cough and expectorate, and the early detection of such cases depends on the general practitioners. Even though screening of the population for tuberculosis is carried out on an enormous scale nowadays, the majority of the infectious cases are still detected among persons referred to the chest clinics by the general practitioners. The co-operation between family doctor and chest clinic is regarded as the cornerstone of the case-finding work. The clinics, therefore, do not examine individual patients attending for the first time without a reference from their private doctor, and the referring doctor is informed of all examination results. The general practitioners have come to regard the chest clinics as allies to whom they can turn for help and advice. Domiciliary treatment takes place — if at all — in consultation with the tuberculosis specialist.

Owing to the routine examination of the general population, the number of persons referred to the chest clinics by their private doctors because of general or chest symptoms account for less than 10 per cent of the total number of adults examined, but still 60 per cent of all new adult cases and approximately 70 per cent of those with a positive sputum are found among these referrals.

B. Examination of contacts.

Whenever a new case of tuberculosis is diagnosed, or merely a positive tuberculin reaction is observed in a non-vaccinated child, the chest clinic makes an examination of all contacts in the household, among acquaintances and at the place of work. For these examinations no reference from a physician is required, but the private physician of each person examined is informed of the reason for the examination, the result of the examination and of any measures taken. The contact examination is not only carried out locally but is extended to members of the family living in other parts of the country. This is presumably the reason why in Denmark, before the mass-vaccinations, we were so familiar with the epidemic occurrence of tuberculosis, a phenomenon that our visitors from abroad often claim is unknown to them. Minor epidemics in families or among acquaintances were often brought to light by exhaustive contact examinations.

The "contact" group includes 4 per cent of the adults examined and 9 per cent of the new cases discovered.

C. Examination for other reasons. (Routine examinations).

Some of these examinations are based on specific indications, e. g., the periodic chest x-ray follow-up of diabetics, mental patients and mentally defectives and the routine examination of all medical patients admitted to general hospitals carried out by many chest clinics in the provinces.

However, the vast majority of the routine examinations are group examinations of healthy people. A certain percentage of these are carried out among children, adolescents, teachers and personnel at child-welfare institutions as a compulsory part of the general health supervision of children and as a protective measure, while the majority are carried out as a more or less well-founded service to selected groups of the population, chiefly the staffs of large firms or institutions.

Mass campaigns aimed at the whole population of a particular area have been carried out on Bornholm in 1936—40. In the metropolitan area in 1946—48, and in the rest of the country in 1950—52. Further county-wide mass surveys are being conducted by the chest clinics in areas where tuberculosis is still comparatively prevalent.

The routine examinations account for 87 per cent of adults examined and for 29 per cent of new cases found.

Table 2.

Number of Adults Examined at the Chest Clinics, and Number of New Cases of Respiratory Tuberculosis Diagnosed, by Reason for Examination, Denmark 1954.

Reason for examination	Persons Examined	New cases of respiratory tuberculosis	
	No.	No.	Per 100,000 persons examined
Symptoms	72,000	822	1,140
Contact with tuberculosis	36,000	123	340
Mass x-ray and other reasons	707,000	393	56
Total examined ..	815,000	1,338	164
Total adult population:	3,200,000		
New cases:		1,338	
New cases per 100,000 population:			42

Table 2 gives morbidity rates for the three examination groups and for the total population*); the contribution made by the general practitioners is of decisive importance for tuberculosis control; the routine examinations are still an important supplement, but the selection of population groups for routine examination, however should, doubtless be made according to stricter epidemiological criteria than has been the case.

BCG VACCINATION

The proper place of BCG vaccination in tuberculosis control is a subject of controversy in

*) The figures for new cases are as yet preliminary, but such corrections as may become necessary will not materially change the essential features.

many parts of the world; very likely the vaccine and the value of vaccination has, in fact, varied markedly from country to country. After many years of cautious and gradually extended application, BCG vaccination has become a natural part of general tuberculosis control in Denmark. Although the increase in resistance resulting from vaccination may by rather small, we regard it as a useful supplement that may be given to the entire population with ease and little expense.

It is incontestable that BCG has an immunizing effect in animals, as shown by inhibition of multiplication and spread of virulent tubercle bacilli in the tissues of vaccinated animals; epidemiological and clinical experience suggests that BCG has a corresponding effect in human beings, giving considerable protection against the earlist manifestations of virulent infection: primary tuberculosis of the lungs (which not infrequently progresses directly to a phthisis), meningitis and miliary tuberculosis. Presumably some protection is obtained also against late chronic pulmonary tuberculosis; one would expect the inhibition of bacterial multiplication to reduce the number of surviving resting tubercle bacilli and consequently decrease the chances of a late endogenous reinfection, but our experience in this respect is slight.

Progressive primary tuberculosis in the younger age groups, however, has been of enough importance in our total tuberculosis morbidity that protection against this form alone is regarded as a valuable aid; and the risk of infection for young adults is still so great that we hold that all children should be vaccinated before they leave school. To restrict vaccination to those living in a tuberculous environment seems irrational to us, as the spread of infection takes place largely before the source case is detected. If vaccination is considered at all important, then it is obviously best to anticipate the exposure to infection unless the drawbacks of vaccination contraindicate its general application. In infants and small children the inconveniences resulting from a strongly immunizing vaccine are relatively great, and the risk of exposure is in general so slight that in this age group we consider it reasonable to limit vaccination to particularly exposed groups.

K. A. Jensen (4) introduced BCG in Denmark in 1927, and it was only after he had established the necessary confidence in this prophylactic through his experimental work and extensive practical trials that the chest clinics began to vaccinate heavily exposed contacts. Apart from an early experimental mass vaccination campaign on the island of Bornholm in 1936—40 (H. Chr. Olsen) (7), the field of application was extended only gradually, and as late as 1945—46 only about 100,000 or 2.5 per cent of the population had been vaccinated. (Fig. 3). Scientifically adequate control studies were unfortunately not carried out, but our experience with the vaccine was good, as clearly illustrated by the famous school epidemic reported by Hyge (3), and a strong demand for a general mass vaccination was made. A vaccination campaign covering the whole country was then carried out in connection with the aforementioned mass examinations and in connection with the school health examinations.

By the end of 1953 nearly one-third of the total population had been vaccinated; in the most important age groups, 15—29 years, only 5 to 10 per cent were vaccinated by 1945, 60 per cent by 1953.

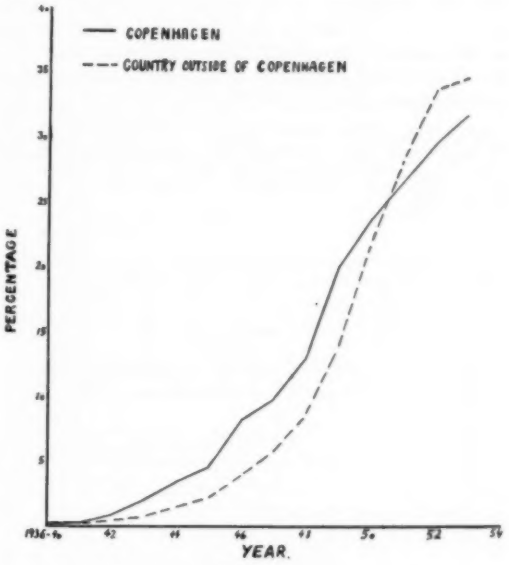

Fig. 3.
Cumulated number of BCG vaccinations per 100 population, Copenhagen and Denmark outside Copenhagen 1936—53.

The systematic vaccination of the rising generation is based on our School Health Act. In a provision that came into force on April 1, 1949, this Act stipulates that all school children, through co-operation between the School Health Officer and the chest clinic, shall be examined for tuberculosis and that all tuberculin-negative children shall be offered BCG vaccination before they leave school. It has become accepted practice to vaccinate the children when they enter school at the age of 7, to re-test them before they leave school and to re-vaccinate the few who are tuberculin-negative. Vaccination is almost uniformly accepted, the vaccination rate for tuberculin-negative school children being about 97 per cent in the provinces and about 90 per cent in Copenhagen.

In non-exposed pre-school children systematic vaccination is carried out only on a limited scale. Well over half of the children below school age attend the prophylactic health examinations conducted by general practitioners. These include annual tuberculin testing, starting at the age of

10 months; in the urban districts where tuberculosis is still comparatively prevalent, the tuberculin-negative children are, as a rule, referred to the chest clinics for vaccination.

All BCG vaccination in Denmark is and always has been voluntary.

INFECTION RATE, MORBIDITY AND MORTALITY

The incidence of tuberculosis infection can still be followed fairly well up to the age of 7 years; above this age the vaccinations have made it impossible to use the tuberculin test for this purpose. At the age of 7 years the proportion of infected children — as measured by a single Mantoux 10 TU test — is today 0,5 to 5 per cent. In the epidemiological surveys carried out by the State Serum Institute in the mid-thirties, this percentage was found to be 5 to 15 per cent in areas free from tuberculosis among cattle and 25 to 50 per cent in areas with cattle tuberculosis (Th. Madsen, Johs. Holm and K. A. Jensen) (6).

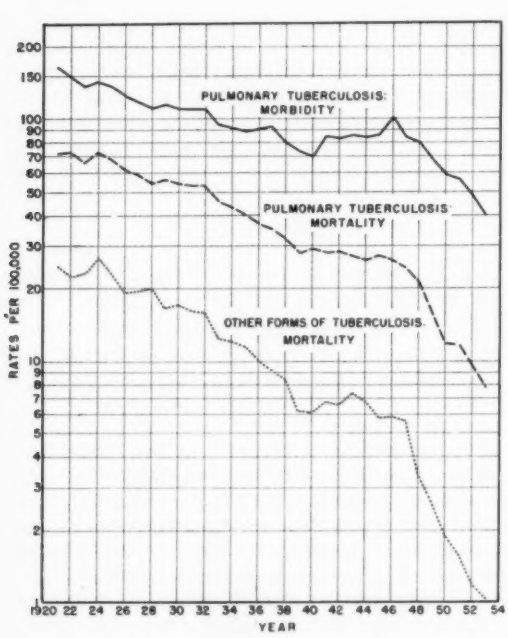

Fig. 4.

Morbidity and mortality from pulmonary tuberculosis and mortality from non-pulmonary tuberculosis, Denmark, 1921—53.

Tuberculosis mortality among the urban population has been recorded since 1876. In that year mortality from all forms of tuberculosis was well above 300 per 100,000 population (Marie Lindhardt) (5). Apart from a steep rise during the First World War, the mortality has shown a continuous downward trend ever since 1890; in 1954 it was 7.7 per 100,000 for the total population.

Detailed country-wide tuberculosis morbidity and mortality statistics are available since 1921; see Fig. 4 and Horwitz & Iversen, page 173 in this issue of the *Danish Medical Bulletin*.

It is notable that the morbidity and mortality curves for pulmonary tuberculosis run almost parallel throughout the period 1920—32 but then they diverge, the number of new cases per death increasing from 2 in 1932 to 4 in 1946. This change is in part due to local increases in the tuberculosis morbidity registered after the establishment of the local chest clinics. A particularly interesting point is that the rapid fall in mortality that has been observed all over the world since 1948 is accompanied in Denmark by a spectacular decrease in tuberculosis morbidity. Since 1948 the mortality has on the average decreased by 18 per cent annually and the morbidity by 13 per cent in incidence rate.

It has been feared that the chemotherapy might cause an increase in the number of surviving but still infectious patients.

The best obtainable index of the prevalence of pulmonary tuberculosis in a given year is undoubtedly the number of patients alive and sputum- or gastric lavage positive in that year. For the years prior to 1949 this information or similar information is available for a few chest clinic areas only. The Copenhagen chest clinic has thus each year reported the number of patients in whom tubercle bacilli have been demonstrated within the last three calendar years. This figure went up from 3061 in 1940 to 4548 in 1948 and has since decreased year by year to 3560 in 1953. Available figures from a few provincial chest clinics show a corresponding trend.

From 1949 information on the total number of known "bacillary" patients in each calendar year is available for the greater part of the population in the provinces, i. e., for an area with a population of 3 million in 1949.

In this area the total number of registered patients reported sputum- or gastric lavage positive during the calendar year was:

Year	Absolute number	Per 100,000 population
1949	4112	134
1950	4210	136
1951	3831	123
1952	3479	111
1953	3488	110
1954	2656	82

According to the above figures, the fear that the tuberculous population might be on the increase because modern chemotherapy augments the number of surviving but still infectious patients seems unfounded. Since 1948—50 there has been a definite decrease in the number of known infectious patients.

COMMENTS

The cause of the decline of tuberculosis since the 'eighties is no more known in this country

than elsewhere. It is not possible to single out any particularly effective factors, but we would guess that the general improvement in living conditions — housing, working conditions and nutrition — has been crucial, that education of the public as to the infectious nature of the disease has been of some importance, but that the other direct control measures have played a secondary part until recent years. That Denmark already in the early thirties was among the nations with the very lowest tuberculosis mortality cannot be attributed to the fight against tuberculosis in cattle nor to the work of the chest clinics nor to BCG vaccination, for the effect of these factors cannot possibly have manifested itself so early, although they may be of importance for our position today.

The spectacular fall in tuberculosis mortality that has taken place since 1948 is universal and is undoubtedly mainly due to a decrease in lethality, a distinct effect of therapy never seen before.

At the same time, the morbidity has remained rather constant in many countries, but this may be due, in part at least, to the fact that the morbidity figures now may include an appreciable number of mild, spontaneously curable or chronic benign cases detected through the extensive use of mass radiography since the war. In Denmark, too, mass radiography has been used since the war on a much larger scale than ever before; nevertheless, we have experienced an unusually rapid decrease in tuberculosis morbidity ever since 1946. It is reasonable to conclude that the ordinary case-finding work of the general practitioners and the chest clinics was efficient enough to disclose the great majority of all cases of tuberculosis even before the mass examinations.

It also has to be emphasized that since 1946 tuberculosis in cattle has been definitely eradicated, the population has been systematically vaccinated and the dependents of the patients have been secured a higher level of social security.

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THE ERADICATION OF BOVINE TUBERCULOSIS IN DENMARK

A SURVEY

By N. PLUM

Three main factors have proved decisive in attempting the gigantic task of eradicating bovine tuberculosis from Denmark:

1) The veterinary administration (The Veterinary Directorate of the Ministry of Agriculture) in co-operation with
2) the separate agricultural organizations, and
3) adequate funds for tackling a problem of this nature and extent.

The initial ground work of Danish veterinarians in the fight against bovine tuberculosis was begun as far back as 1891 when B e r n h a r d B a n g carried out his first experiments in elucidating the diagnostic value of tuberculin in combating bovine tuberculosis. Based on the satisfactory results he obtained, B a n g opened his campaign for the eradication of bovine tuberculosis. He advised farmers to isolate their newborn calves and to build up healthy herds from this new stock, using the tuberculin-test to ensure that the growing animals remained healthy (the so-called Bang method).

As, at that time, only the subcutaneous test (thermo-reaction) was at disposal, the tuberculin-test was in itself a circumstantial matter involving numbers of measurements of body temperature, and thus B a n g enlisted the co-operation of relatively few adherents, most of them on big farms, where better space made for more effective isolation.

During the years that followed, the idea of eradicating tuberculosis admittedly obtained more adherents, but it would be untrue to say that farmers viewed B a n g's campaign with the sympathy it rightly deserved.

In 1898 a law was passed enacting that cows suffering from tuberculosis of the udder (tuberculosis of the uterus was later included) should be destroyed at public expense, and in the same

From the State Veterinary Serum Laboratory, Copenhagen

year a bill ordering the pasteurization of all milk returned from the dairies to the farmers for feeding their stock was also enacted. These measures, however, did not substantially stimulate the campaign.

In 1910 M. Christiansen demonstrated the value of the intracutaneous tuberculin-test as applied to cattle. Interest in the matter now revived, since tuberculin-tests were much easier to carry out by this means than by the former method.

However, it was not yet possible to start a coordinated campaign against bovine tuberculosis. The reason for this was that those who tried met with so many disappointments, either because it so happened that the reacting animals did not have tuberculosis, or because the animals isolated according to the Bang method nevertheless contracted tuberculosis owing to inefficient isolation. It was also of some consequence that the tuberculin-test, to a certain extent, was brought into discredit by certain persons who deceitfully immunized tuberculous animals, so that they did not react to the test. However, even if the tuberculin-test was carried out *lege artis*, be it by subcutaneous or by intracutaneous method, too many mistakes were made in carrying out the tests, and it goes without saying that this fact was avidly utilized by opponents to the idea of eradicating bovine tuberculosis.

Nevertheless, some individual veterinarians engaged in general practice (among them N. O. Nielsen of Remkolde and L. Ramvad of Ringe) succeeded in carrying through a regular eradication within their districts, but no general, organized eradication of bovine tuberculosis took place.

The reason for the lack of proper organization was largely due to the ever recurring discussions as to which of the tests — the subcutaneous test or the intracutaneous test — was the better method, and which reaction — when considering the intracutaneous test — was to be regarded as positive. Some held that every recognizable increase in the thickness of the skin after an injection of tuberculin was to be regarded as a positive reaction, whereas others held that only animals showing an increase of 4 mm in the thickness of the skin should be regarded as reactors.

During the twenties the discussions between adherents and opponents of the tuberculin-tests as a basis for the eradication of bovine tuberculosis grew ever more acrimonious, and it was evident that it was the duty of the Veterinary Directorate to put matters right regarding the carrying out and the evaluation of the tuberculin-test.

It was only natural that it was the State Veterinary Serum Laboratory that eventually elucidated the course and nature of the tuberculin sensitivity in cattle by infection with different types of tubercle bacteria, since, in 1925, a paper from this laboratory on abortion in cattle caused by infection with avian tubercle bacteria had thrown light on an essential source of error in the intracutaneous tuberculin-test.

In this paper it was demonstrated that, in a herd free of bovine tuberculosis, cows could be found aborting after an infection of the uterus by avian tubercle bacteria. These and other animals in these particular herds reacted to bovine tuberculin in spite of their not being infected by bovine tubercle bacteria. Further investigations showed that animals taking up avian tubercle bacteria in many cases reacted to bovine tuberculin by the intracutaneous test. After slaughtering these animals, minor lesions, from which avian tubercle bacteria could be isolated, were found in the mesenterial lymph glands in several instances, while in others absolutely no tuberculous lesions could be demonstrated in any organ.

The research work of the Serum Laboratory resulted in a series of papers concerning the proper technique for the tuberculin-test and the judging of the herd reactions not only by infections with the bovine type of tubercle bacteria, but also by infections with those other types of acid-fast bacteria that in Denmark interfere with the test with bovine tuberculin, i. e., the infections with avian or human tubercle bacteria and with Myc. paratuberculosis. The work of the Laboratory also included investigations into the extremely contagious and not easily diagnosed genital tuberculosis of cattle, and into the diagnosis of several other manifestations of tuberculosis. Finally, a proposal was outlined as to how to carry through an eradication embracing the whole country.

Based on these works, the Veterinary Directorate (*Gerhard Petersen*, then Veterinary Inspector and later Veterinary Director), in co-operation with the Laboratory, worked out by-laws and instructions for the carrying out of the tuberculin-test, etc., approved and issued by the Ministry of Agriculture in 1932.

The central ideas of said by-laws are as follows: Only tuberculin issued by the State Veterinary Serum Laboratory may be used by veterinary surgeons. The intracutaneous test is made compulsory, and definite rules are laid down as to the site of injection, the amount of tuberculin to be used, and the right moment for measuring the results.

It is also stipulated as to when re-tests with bovine as well as avian tuberculin should be carried out. The measuring of the skin must be carried out with calipers approved by the Veterinary Directorate, and the results of all tests must be sent to the Veterinary Directorate through the District Veterinary Officers. Certificates concerning tuberculin-tests must be issued on authorized forms, and veterinary surgeons are not allowed

to make additional remarks on the forms which they have merely to fill out as prescribed.

Some anxious curiosity was felt as to how these regulations would be received by veterinary surgeons and farmers, since it was the first time, to our knowledge, that the State had issued definite rules as to the carrying out of a scientific, diagnostic test. Also the form of the certificate was made so precise that no personal interpretation on the part of veterinary surgeons was possible.

However, as it appeared, everyone was forced to admit that the introduction of these strict regulations was justified. Thus 1932 should be regarded as the year when properly organized eradication of bovine tuberculosis was really begun.

Apart from the introduction of regulations of purely organizational value, the turning point in a scientific respect was that, from now on, it was not merely sufficient to state that an animal reacted to an intracutaneous test with bovine tuberculin, but it was also desirable to know why it so reacted, so that it might be possible to separate cattle reacting from other causes than infection with bovine tuberculosis.

The leading principle was that a stricter standard had to be adopted in herds known to be infected with bovine tuberculosis than in herds known to be free from tuberculosis. At the same time, not only the reaction in an individual animal but the reactions in the herd as a whole had to be considered, and by re-tests, using bovine as well as avian tuberculin, those reactors were pointed out that were not infected with bovine tuberculosis and therefore should remain in the herds.

The procedure in making tuberculosis investigations was, hereafter, that veterinary surgeons might apply to the Veterinary Directorate for tuberculin, which was then issued by the Serum Laboratory. When the tests had been carried out, the results were sent to the District Veterinary Officer, who judged the results and, if necessary, had a consultation with the veterinary surgeon as to further measures.

The result of the test was then sent on to the Veterinary Directorate, where a register is kept of all tuberculin-tests carried out in this country. When a herd could be certified free from bovine tuberculosis, it was entered — at the decision of the Veterinary Directorate — in the register of tuberculosis-free herds, which register is kept by the Joint Organization of the Co-operative Dairies. The Veterinary Directorate likewise decided when a herd on re-infection was to be removed from the register.

Thus, the Veterinary Directorate took complete charge of the eradication of bovine tuberculosis in Denmark, and it was an enormous amount of work that hereafter had to be shouldered by the administration.

The position as District Veterinary Officer was established in 1928, when a handful of veterinary surgeons were invited for a nominal salary to supervise the efforts of the Veterinary Directorate in combating bovine tuberculosis. However, as the campaign gained momentum, they were employed as civil servants holding a full-time post under the Veterinary Directorate.

Thus, from that time on, thousands of applications had to pass the Veterinary Directorate and hundreds of thousands of tuberculin-tests had to pass the District Veterinary Officers every year. At the same time, thousands of type determinations were carried out at the State Veterinary Serum Laboratory to confirm results of tuberculin tests.

Even if the work of eradicating bovine tuberculosis had been and still was founded on a voluntary basis, it expanded at such a rate that, in about 1937, the campaign covered the entire country. The results obtained were so good that, in 1942, a law was passed with a view towards completing the eradication of bovine tuberculosis as quickly as possible.

The by-law issued by the Ministry of Agriculture in 1932 already included provisions for demanding a compulsory test of the remaining herds in a co-operative dairy when 90 per cent of its herds were healthy. The reactors to this test had then to be ear-marked and possibly slaughtered. Likewise, provision had been made for the issue of a prohibitory decree precluding the importation of cattle not definitely known to be free of tuberculosis into circumscribed tuberculosis-free districts, and as these decrees proved insufficient, further restrictions had to be imposed according to the law passed in 1942.

Thus, strict regulations were introduced prohibiting the grazing of cattle from a tuberculous herd near healthy stock. The use by such cattle of watering places in common with healthy stock was likewise prohibited.

Before the passing of this law, it was the owner of the healthy herd that had to take measures to protect his cattle from infection by tuberculous animals. According to the new rulings, all responsibility for infection of healthy stock was put on the owner of the tuberculous herd.

Dairies that had not yet joined the authorized eradication scheme were to reduce the price of milk from herds, not yet free of bovine tuberculosis, and special markets for tuberculosis-free animals were established.

It was decided that the Ministry of Agriculture should be authorized to order heavily infected tuberculous herds to be slaughtered at public expense. This regulation, however, was never brought into force for even the most rabid opponents came around after the passing of the law and joined the voluntary eradication scheme.

The final result of all these regulations was, that in June 1952, Denmark could be declared

free of bovine tuberculosis, and at the same time it was decided that a dairy only should be allowed to use the State-guaranteed trade mark, the "Lur brand" on the condition that only milk from herds declared free of bovine tuberculosis would be accepted at the dairy.

This decision was a drastic measure, because butter and cheese could only be legally exported when these products were stamped with the "Lur brand". The practical consequence of this decision is that, if a single milk producing farmer within a dairy district has a reactor in his herd, the dairy in question will not be allowed to export either butter or cheese.

The regulations mentioned above (laws and by-laws and instructions) could not have been carried through without the consent of the farmers, and they have all been worked out in close co-operation with the various agricultural organizations, among which the dairy organizations have, as a matter of course, played a major role. In their efforts to carry the movement to a successful issue, the dairy organizations took up Mr. L. R a m v a d's ideas of 1920, *viz.*, to conduct the campaign against bovine tuberculosis within individual dairy districts. This was a happy idea, and one which has materially contributed to the success of the campaign.

It was of essential importance that after the organized fight against bovine tuberculosis had got well under way, the agricultural organizations — and again primarily the dairy organizations — instituted a large amount of educational work directed by the Bureau of the Joint Organization of the Co-operative Dairies in Aarhus. The instruction was given by the advisors of hygiene of the organization, who gave instructional lectures and showed illustrative films.

The third factor in the combat was the question of how to provide the large sums of money necessary to be able to offer at least some damages to the farmers that joined the movement to eradicate tuberculosis. As early as 1893 public funds were put at disposal for carrying out the tuberculin-tests in cattle, and, likewise, compensation was given for cows slaughtered through having contracted tuberculosis of the udder or the uterus.

In 1934 the Government made further monetary means available for the slaughtering and destroying of cows during the agricultural crisis of those days. However, it was not long before part of the money was appropriated for combating bovine tuberculosis, that is to say, it was chiefly only tuberculosis animals that were slaughtered and destroyed.

However, the farmer's organizations soon took over the lion's share of the huge expenses connected with these slaughterings by putting a duty on all export of meat and live cattle. These means were collected in a fund that was used to cover the expenses incurred in paying damages to farmers who cleared their herds of tuberculosis. Thus it is the farmers themselves who, to a great extent, have covered the expenses incurred in the campaign against bovine tuberculosis.

The exact sum of money used during the campaign through the years is difficult to assess. It must run into millions, but everybody will probably be able to see that the investment has paid and will pay many times over in the future.

These, then, are the main features of the gigantic fight against bovine tuberculosis in Denmark, a fight that was concluded in 1952. The campaign was carried through under the direction of the Veterinary Directorate, headed by F. W ø l d i k e N i e l s e n, Veterinary Director, during the concluding phase.

This excellent result is a fine example of what can be done in combating an infectious disease in domestic animals by well-organized co-operation between science, veterinary administration and agricultural organizations on a rational basis.

It is evident that, for several years to come, re-infections will appear in our herds, in great part through contamination from human beings suffering from bovine tuberculosis. In this connection it is, however, of interest to note that, in 1953, only 24 re-infections made their appearance — chiefly owing to the fact that infections with bovine tuberculosis among humans are now definitely on the decrease.

Thus Dr. L. E n g b æ k, of the State Serum Institute, reports, that while in 1940 140 cases of bovine tuberculosis in human beings were diagnosed, this figure fell to 47 in 1953 among patients examined for the first time.

The course of the campaign from the year 1937 — when all Danish herds had joined the eradication scheme — is given in the following table.

Tuberculosis-free herds in per cent.

	Islands	Jutland	All of Denmark
1937	38,1	19,7	26,5
1938	57,1	27,1	38,6
1939	68,4	32,3	45,4
1940	80,8	39,4	54,2
1941	88,5	46,4	61,7
1942	93,6	58,9	71,2
1943	96,6	71,3	80,3
1944	99,1	79,4	86,3
1945	99,9	86,3	91,1
1946	99,9	90,5	93,9
1947	99,9	96,0	97,4
1948	100,0	98,8	99,2
1949	100,0	99,5	99,7
1950	100,0	99,6	99,7
1951	100,0	99,9	99,9
1952	100,0	99,9	99,9

THE INCIDENCE OF PULMONARY TUBERCULOSIS IN DENMARK 1921—1953

By OLE HORWITZ and ERIK IVERSEN

INTRODUCTION

The incidence of pulmonary tuberculosis in Denmark may be studied on the basis of morbidity as well as mortality statistics. Up to the present, however, the main stress has been laid on the mortality statistics, as the morbidity statistics have been considered somewhat unreliable. One reason for this is the dependence of morbidity statistics on the extent of medical examination in the population (i. e., how many of those with the disease are seen by a doctor) and on the completeness of notification (i. e., how many of the cases diagnosed are notified to the health authorities). Mortality statistics are far less dependent on these factors, as each death is registered and the cause of death in each case is indicated by the physician issuing the death certificate.

As long as the relation of the number of new cases of the disease to the number of deaths remains reasonably constant, the mortality figures accurately reflect changes in the incidence of tuberculosis. However, in recent years the relation has changed in that the mortality has decreased more than the morbidity. The mortality figures thus no longer give an accurate expression of the changes in morbidity and may easily result in an underestimation of the social importance of tuberculosis. Moreover, the mortality has gradually fallen to such a low level that break-downs of the number of deaths, e. g., by sex and age, will result in very small figures markedly affected by random fluctuations. Future evaluations of the incidence of tuberculosis should therefore be based also on morbidity rates.

One of the purposes of the study reported here has been to compare tuberculosis morbidity and mortality to determine to what extent they present common features. Other aims have been to examine the time-trend and certain geographic differences; this is partly of a general epidemiological interest and partly of interest as a background for the studies on tuberculosis in selected population groups conducted by the Danish Tuberculosis Index.

The crude rates used in the present paper are to some extent affected by variations in the age and sex structure of the population. A preliminary analysis of the rates by sex and age groups has, however, shown that the characteristic features found are real, that is, that they are largely independent of variations in the age and sex composition of the population.

From the Danish Tuberculosis Index. Chief: *E. Groth-Petersen.*

MATERIAL

The present study is based on the annual morbidity and mortality statistics of the National Health Service (8, 9). Rates per 100,000 population have been computed from the number of notified cases of pulmonary tuberculosis and the number of deaths from pulmonary tuberculosis, respectively, and the corresponding population figures reported in the above publications.

A detailed description of the basis for these statistics has been given by Lindhardt (2, 3) and in the Medical Report (9) for 1951. Certain aspects that are of importance to the present study will be discussed below.

Morbidity statistics. Since 1905 every Danish physician has been bound by law to report to the National Health Service all persons with tuberculosis in the lungs or larynx treated by him (Act of April 14, 1905, section 2). Throughout, the notifications have been made on individual forms. Regular statistical processing of the notifications was begun in 1920 and at the same time a central register for all notified cases was set up. By matching all incoming notifications against this central register, re-notifications could be sorted out and the same case was thus prevented from appearing more than once in the statistics.

As the register only included cases notified after 1920, the number of notifications for the first years was somewhat too large in that it included re-notifications of cases reported before 1920. Throughout, all cases reported dead have been removed from the register. Moreover, in 1930 it was decided to remove notified cases 8 years[1]) after the first notification (if they had not been removed earlier because of death) in order to compensate for the fact that cured cases could not be removed from the register. As a result, the notifications for the years after 1930 include a certain number of cases re-notified after an interval of more than 8 years; the notification figures were thus still somewhat too high.[2]) Be-

[1]) On the basis of various investigations (Lindhardt, 2, pp. 23—25) the hypothesis was formulated that the average duration of disease for tuberculous patients was 8 years.

[2]) This is one of the reasons why the figures for tuberculosis morbidity are slightly higher in the Medical Reports (9) than in the tabulations from the tuberculosis dispensaries.

ginning 1951 this procedure has been changed so that cases are now removed from the register only on death, emigration or cure (annual reports from the tuberculosis dispensaries).

The morbidity figures include, in addition to the above-mentioned notified cases of pulmonary tuberculosis, all persons who have died from pulmonary tuberculosis without their disease having been notified before death. The latter group comprises: (1) cases only diagnosed at the time of death; (2) diagnosed cases which by mistake have not been notified; (3) cases notified before 1920 and — for the period 1930-50 — cases notified more than 8 years before death. The proportion of cases notified only at the time of death decreased during 1944-53 from 13 to 2 per cent of the total number of new cases. Corresponding figures for the earlier years are not available, but during 1925-34 about 20 per cent of the cases were notified less than 30 days before death (L i n d h a r d t, 2, p. 29).

In 1940 new sections were introduced into the notification forms for the recording of data on the severity and character of the cases, e. g., the results of bacteriological examinations made at the time of notification. The proportion of bacteriologically positive cases increased between 1943 and 1953 from 76 to 88 per cent.

Mortality statistics. After every death a death certificate is issued stating the cause of death. The entries on cause of death are practically always either made or verified by the physician who was last treating the deceased. The National Health Service, on the basis of the death certificates, prepares the annual statistics of causes of death which have been published since 1876 for the towns and since 1920 for the rural districts. The changes made in the classification of causes of death[3]) have presumably had only little influence on the death rate for pulmonary tuberculosis (L i n d h a r d t, 5).

PULMONARY TUBERCULOSIS MORBIDITY AND MORTALITY IN DENMARK

The main trends of pulmonary tuberculosis morbidity and mortality appear from Fig. 1, which — on logarithmic paper[4]) — gives morbidity and mortality curves for the entire country for the years from 1921 to 1953. In Table I this period has been divided into shorter periods, within which the curves in Fig. 1 run fairly straight with a constant percentage rise or fall). For each of these periods Table I gives the initial and the terminal morbidity and mortality rates as well as the annual percentage increase or decrease of the rates.

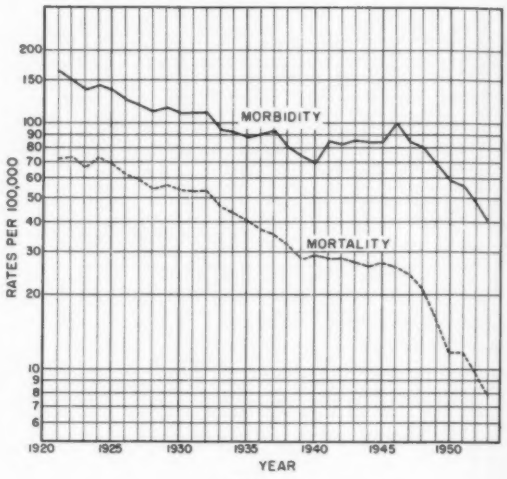

Fig. 1.
Morbidity and mortality from pulmonary tuberculosis 1921—53. All of Denmark.

It is seen that both the morbidity and the mortality from pulmonary tuberculosis declined during the first two decades. Throughout the

[3]) Up to 1930 the Danish classification of 1875 was used, during 1931—40 the Scandinavian classification of 1926 and from 1941 to 1950 the international classification of 1938; in 1951 the classification prepared by the WHO was introduced.

[4]) For the information of readers not versed in mathematics it should be mentioned that curves drawn on *logarithmic paper* give an immediate impression of the *relative* changes in the rates — in contrast to curves drawn on *ordinary scale paper* which show the *absolute* changes. Thus on logarithmic paper the distance between 200 and 100 is the same as between 16 and 8: in both cases one rate is twice as high as the other.

Table I.
Changes in pulmonary tuberculosis morbidity and mortality in selected periods between 1921 and 1953. All of Denmark.

MORBIDITY				MORTALITY			
Period	Initial rate	Terminal rate	Average annual change *)	Period	Initial rate	Terminal rate	Average annual change *)
	per 100,000	per 100,000	per cent		per 100,000	per 100,000	per cent
1921—32	163	110	÷ 4	1921—32	72	53	÷ 3
1932—40	110	70	÷ 5	1932—39	53	28	÷ 9
1940—46	70	101	+ 6	1939—45	28	27	÷ 1
1946—48	101	80	÷ 11	1945—48	27	21	÷ 8
1948—53	80	40	÷ 13	1948—53	21	8	÷ 18

*) +: increase; ÷: decrease

twenties they decreased at the same rate, 3—4 per cent per year (the curves in Fig. 1 run parallel), while during the thirties the morbidity decreased by 5 per cent per year and the mortality by 9 per cent (the curves begin to diverge). Around 1940 the downward trend was interrupted: the morbidity increased between 1940 and 1941 and again between 1945 and 1946, remaining constant during the intervening years, while the mortality only showed a very slight decrease between 1939 and 1946. During this period the curves diverge more than before: while the morbidity in 1939 was 2½ times as high as the mortality, it had become 4 times as high in 1946. After the Second World War both curves again show a rapid decline, the morbidity decreasing by about 12 per cent annually and the mortality by 8 per cent per year between 1945 and 1948 and by 18 per cent per year between 1948 and 1953. In 1953 the morbidity was 5 times higher than the mortality.

Whereas the absolute decrease in pulmonary tuberculosis morbidity, from 163 per 100,000 in 1921 to 40 in 1953, is larger than the corresponding decrease in mortality, from 72 to 8 per 100,000, the largest relative decrease during most of this period was shown by the mortality. Altogether the morbidity was reduced by 75 per cent and the mortality by 89 per cent.

In summarizing it can be said that the pulmonary tuberculosis morbidity and mortality curves present two characteristic features:

1. The curves show largely the same form: the rates decreased fairly rapidly during the twenties and thirties, increased or showed only a slight decrease from 1940 to 1946 and thereafter declined more rapidly than ever before.

2. The mortality curve, however, shows a larger total decrease than the morbidity curve.

That the morbidity and mortality curves are similar in form may seem surprising. One would have expected in the case of a largely chronic disease such as pulmonary tuberculosis that a change in the trend of the morbidity curve would be followed by a corresponding change in mortality only after an interval of some years. That the two curves instead show a change in trend about simultaneously at the beginning of the war may perhaps be explained by a decrease in resistance partly in the general population (leading to a rise in morbidity) and partly in the tuberculous patients (leading to a rise in mortality).

That the morbidity curve has declined less than the mortality curve may in part be due to an artificial increase in the morbidity figures: the marked increase in the activity of the tuberculosis dispensaries has led to the detection of many mild cases which in earlier years might have remained undiagnosed; in addition, the setting-up of tuberculosis dispensaries has resulted in a more complete registration of new cases. Another thing is that improvements in therapy may have resulted in that fewer tuberculous patients die from their disease.

COPENHAGEN, PROVINCIAL TOWNS AND RURAL DISTRICTS

It is well known — see, e. g., Ostenfeld (6, 7) and Lindhardt (2, 4) — that tuberculosis is more frequent in urban than in rural areas. Morbidity and mortality rates are therefore given separately for Copenhagen, the provincial towns and the rural districts in Table II and Fig. 2; they correspond to the rates for all Denmark given in Table I and Fig. 1. According to the 1950 census, the three types of district comprised 18, 29 and 53 per cent, respectively, of the Danish population.

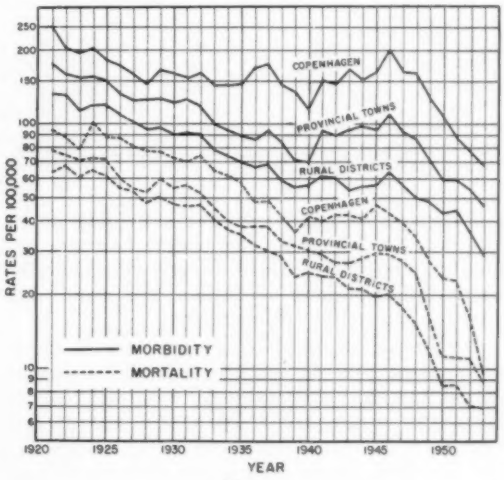

Fig. 2.

Morbidity and mortality from pulmonary tuberculosis 1921—53. Copenhagen, provincial towns and rural districts.

The three types of district have different levels of morbidity and of mortality. Both morbidity and mortality rates, throughout the period under study, are highest in Copenhagen and lowest in the rural districts, while the provincial towns take up an intermediate position. The rates for Copenhagen were at the beginning of the period (the morbidity rates until 1935 and the mortality rates until 1945) 1½ to 2 times and later on 2 to 3 times higher than the rates for the rural districts.

Apart from differences in level the curves for each of the three types of district are very similar to those for all of Denmark. First: even though there are irregularities the morbidity and mortality curves appear to change their trend more or less simultaneously, partly at the beginning of the thirties, partly at the outbreak and at the end of the war. Second: the morbidity and mortality curves run more or less parallel during the earlier part of the period (those for Copenhagen during

Table II.
Changes in pulmonary tuberculosis morbidity and mortality in selected periods between 1921 and 1953. Copenhagen, provincial towns and rural districts.

Period	MORBIDITY Initial rate	Terminal rate	Average annual change *)	Period	MORTALITY Initial rate	Terminal rate	Average annual change *)
	per 100,000	per 100,000	per cent		per 100,000	per 100,000	per cent
Copenhagen							
1921—32	251	160	÷ 4	1921—32	94	74	÷ 2
1932—40	160	114	÷ 4	1932—39	74	36	÷ 10
1940—46	114	199	+ 10	1939—45	36	46	+ 4
1946—48	199	159	÷ 11	1945—48	46	35	÷ 9
1948—53	159	67	÷ 16	1948—53	35	9	÷ 24
Provincial towns							
1921—32	174	117	÷ 4	1921—32	77	52	÷ 4
1932—40	117	69	÷ 6	1932—39	52	32	÷ 7
1940—46	69	109	+ 8	1939—45	32	29	÷ 2
1946—48	109	85	÷ 12	1945—48	29	24	÷ 6
1948—53	85	46	÷ 12	1948—53	24	9	÷ 18
Rural districts							
1921—32	132	90	÷ 3	1921—32	64	46	÷ 3
1932—40	90	56	÷ 6	1932—39	46	23	÷ 9
1940—46	56	63	+ 2	1939—45	23	20	÷ 2
1946—48	63	50	÷ 11	1945—48	20	15	÷ 9
1948—53	50	29	÷ 10	1948—53	15	7	÷ 14

*) +: increase; ÷: decrease

the twenties and those for the provincial towns and the rural districts during the twenties and thirties) and then begin to diverge, the mortality decreasing more (or — during the war — increasing less) than the morbidity.

Certain details in the trend of the curves should be stressed. During the twenties all curves declined, the rates decreasing by 2—4 per cent per year. The downward trend of the curves then became more accentuated, the rates falling 6—10 per cent per annum during the thirties; the sole exception was the morbidity curve for Copenhagen, whose trend was the same during both decades, though with a peak in 1936-37 (perhaps due to the opening of the Copenhagen Municipal Tuberculosis Dispensary). During the war the morbidity went up in all three types of district (most in Copenhagen), and the trend of the mortality curves also changed: in Copenhagen the mortality increased and in the provincial towns and rural districts it decreased less than before. After the war both morbidity and mortality have fallen markedly in all three types of district, the mortality in particular after 1948. It is notable that of the three geographical divisions Copenhagen had both the largest rise during the war and the largest fall after the war while the rural districts show the smallest fluctuations; this applies to both morbidity and mortality rates.

SMALLER AREAS

The epidemiologic studies of the Danish Tuberculosis Index have made it necessary to divide Denmark into regions within which the morbidity and mortality rates are fairly uniform. The division has been made as follows.

Rural districts. A study of the morbidity and mortality curves for the rural districts of the different counties[5]) has shown that three regions — each comprising several counties — may be distinguished:

Western Denmark: comprising North, West and South Jutland.

Central Denmark: comprising Funen and East Jutland.[6])

Eastern Denmark: comprising Zealand, Lolland-Falster and Bornholm.

The position of these regions is shown on the map in Fig. 3.

Fig. 4 shows morbidity and mortality curves for each of the three regions, and for the sake of comparison corresponding curves for Copenhagen and the provincial towns are also given. It is seen that the curve for Western Denmark — and this applies to the morbidity curve as well as to the mortality curve — runs above that for Central Denmark which again runs above that for Eastern Denmark. It is notable that the curves largely maintain their respective positions over a period of more than 30 years. An exception occurred at the end of the forties when, for a short period,

[5]) The rural parts of Copenhagen, Frederiksborg and Vejle counties have been excluded from this study: the rural parts of Copenhagen county because they include several metropolitan boroughs, and those of Frederiksborg and Vejle counties because their rates are markedly affected by the presence of a large mental hospital with patients from all over Denmark (Lindhardt, 2, pp. 46—52).

[6]) East Jutland comprises Skanderborg, Aarhus, Randers, Viborg and Vejle counties.

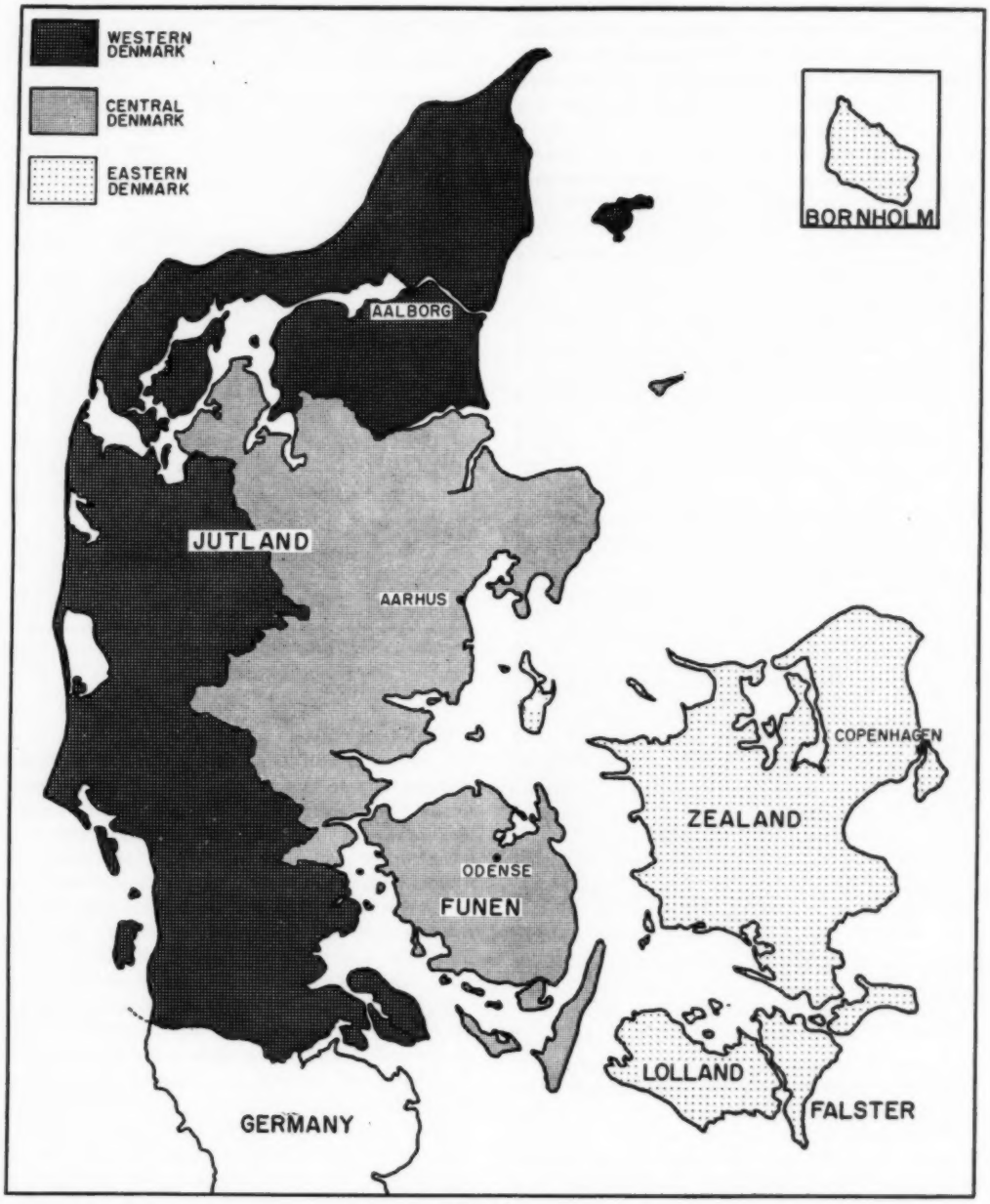

Fig. 3.
Grouping of the counties of Denmark in areas with uniform morbidity and mortality from pulmonary tuberculosis.

the morbidity rates for Eastern Denmark were as high as those for Central Denmark. What Carlsen (1), Ostenfeld (6, 7) and Lindhardt (2) reported about the incidence of pulmonary tuberculosis in the different regions of Denmark during the periods 1906—09, 1920—25 and 1925—34 largely holds good even to-day.

Not only have the curves for the three regions maintained their respective positions throughout the period reviewed, but the intervals between them have remained remarkably constant. Excepting the transitory rise in the morbidity rate for Eastern Denmark in the late forties, it can be said that throughout the three decades the morbidity as well as the mortality rate has been 1½ to 2½ times higher in Western Denmark than in Eastern Denmark, while the rates for Central Denmark have maintained an intermediate level.

This is all the more striking, as the rates themselves have been far from stationary during the three decades: on the average, the morbidity in the rural districts decreased by 78 per cent and the mortality by 89 per cent between 1921 and 1953.

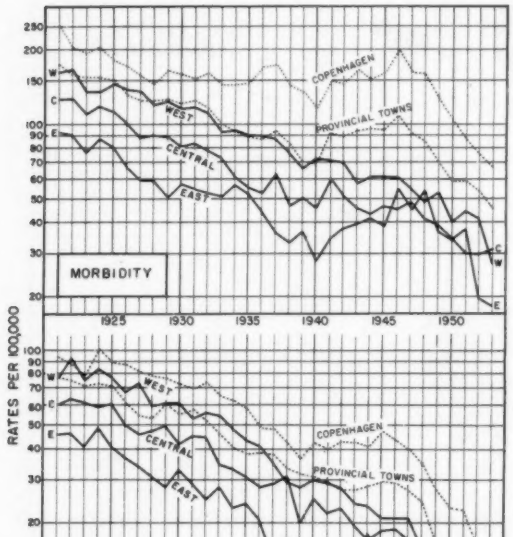

Fig. 4.
Morbidity and mortality from pulmonary tuberculosis 1921—53. Rural districts in Western, Central and Eastern Denmark (compared with Copenhagen and provincial towns).

It should be mentioned that the above features are not seen when the curves for individual counties within the three regions are compared. The rates for such small areas are easily affected by random fluctuations in morbidity and mortality and also by local variations and changes with time in the way notification is practiced.

Towns. When analysing the incidence of tuberculosis in the towns, not only the geographic position of the town but also its size must be considered, cf. Lindhardt (2). The present analysis refers to mortality only, as the official morbidity statistics do not permit grouping of the towns by size. As the urban population outside the capital is fairly small, no curves are given; instead the average annual rates for the three periods 1925-34, 1935-44 and 1945-53 have been computed.

Table III.
Mortality from pulmonary tuberculosis in 1925—34, 1935—44 and 1945—53. Towns of different sizes and rural districts in Western, Central and Eastern Denmark.

Region	Mean annual rates per 100,000 population		
	1925—34	1935—44	1945—53
Capital	73	43	28
Western Denmark			
Aalborg	69	33	23
Other towns of over 10,000	62	33	22
Towns of less than 10,000*)	57	32	16
Rural districts**)	60	31	15
Central Denmark			
Aarhus, Odense	58	33	17
Other towns of over 10,000	53	29	18
Towns of less than 10,000	53	26	15
Rural districts**)	44	24	12
Eastern Denmark			
Towns of over 10,000.	44	27	17
Towns of less than 10,000	45	25	13
Rural districts**)	31	17	9

*) Excluding Ribe where there is a large mental hospital with patients from all over Denmark.
**) See Footnote 5.

Table III gives such rates for the capital (Copenhagen and Frederiksberg municipalities)[7]) and for the towns in each of the three regions found to have a fairly uniform level of morbidity and mortality in its rural districts. The towns have been grouped into large towns[8]), other towns with over 10,000 inhabitants[9]), and towns with less than 10,000 inhabitants. In addition, the table shows — for comparison — the corresponding rates for the rural districts. A graphic presentation of the rates is given in Fig. 5.

It is seen for one thing that the mortality rates of the towns are subject to regional variations corresponding to those shown for rural districts: the rates are highest in Western Denmark and lowest in Eastern Denmark while intermediate in Central Denmark. There is, however, less difference between the towns than between the rural districts of the three regions: the mortality rate for the towns of Western Denmark is 20—40 per cent higher than that for the towns of Eastern Denmark, whereas the rates for the rural districts differ by as much as 65—95 per cent.

Furthermore, it appears that within each region the rates of the towns vary with the size of the town. As a rule, the large towns have higher

7) Population figures 1950: Copenhagen 765,000, Frederiksberg 120,000.
8) Aarhus, Odense and Aalborg; population 1950: 115,000, 100,000 and 80,000, respectively.
9) The largest town had a population of 47,000 in 1950.

rates than the small towns (the capital having the highest rate). However, even the small towns usually have higher rates than the corresponding rural districts.

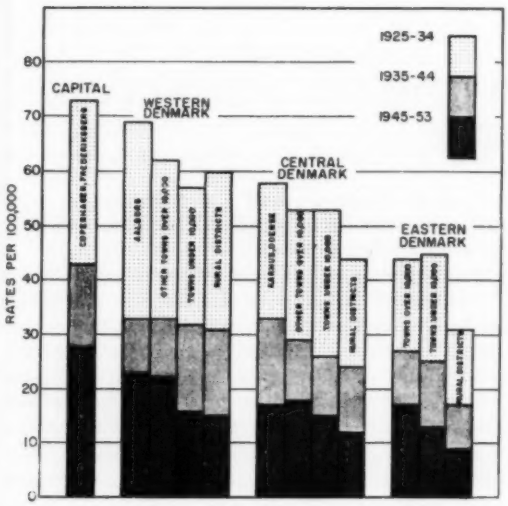

Fig. 5.
Mortality from pulmonary tuberculosis 1925—34, 1935—44 and 1945—53. Towns of different sizes and rural districts in Western, Central and Eastern Denmark.

A correlation between mortality rate and size of town is found in all three regions and for all three periods. During 1925-34 the mortality level of the three major towns differed markedly from that of the other towns, while there was little difference between towns of over and under 10,000. In recent years, however, the difference in mortality rate between towns of over and under 10,000 has become marked, amounting to 20—40 per cent, that is, to as much as the difference between towns of different regions.

SUMMARY AND CONCLUSIONS

The geographical distribution of pulmonary tuberculosis in Denmark has been studied on the basis of the official morbidity and mortality statistics for the years 1921-53. As regards the tuberculosis morbidity statistics, it is of particular importance that in Denmark all cases are notified by physicians on individual forms and filed in a central, nation-wide register.

The case-rate for all of Denmark decreased during the period under study from 163 to 40 per 100,000 and the mortality rate from 73 to 8. Thus, in 1921 there were 2.3 new cases to each death while in 1953 there were 5.0.

The pulmonary tuberculosis morbidity and mortality curves for all of Denmark show largely the same form: the rates went down during the twenties and thirties, rose or decreased only slightly from 1940 to 1946 and thereafter dropped more rapidly than ever before. During the twenties the curves ran more or less parallel, but since the early thirties the mortality has decreased more rapidly (or — during the war — increased less rapidly) than the morbidity.

The curves for Copenhagen, the provincial towns and the rural districts show by and large the same trends as the curves for all of Denmark, but their levels differ. Both the morbidity and the mortality rates are 1½ to 3 times higher in Copenhagen than in the rural districts, the rates for the provincial towns running at an intermediate level.

Grouping of the rural districts into three geographical regions — West, Central and East — shows that in "Western Denmark" the rural morbidity and mortality rates during most of the period considered were twice as high as in "Eastern Denmark", while in "Central Denmark" the rates were somewhere in-between.

In the towns the mortality rate depends partly on the geographical position — as did the rates in the rural districts — and partly on the size of the town. The larger the towns, the higher the mortality rates.

It appears from the study that the most important difference between the trends of pulmonary tuberculosis morbidity and mortality is that the latter has decreased more rapidly than the former. Apart from this difference the trends have for more than 30 years been strikingly uniform. Moreover, breakdowns of the rates by type of district — urban and rural — and according to geographical position reveal the same pattern whether one looks at the morbidity or at the mortality. This parallelism is of great interest, as the rapid reduction in tuberculosis mortality will make it necessary to attach more importance to the morbidity figures in future studies of the epidemiology or the social importance of tuberculosis.

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THE TREATMENT OF EXTRAPULMONARY TUBERCULOSIS

By HANS THOMSEN

The treatment of extrapulmonary tuberculosis in Denmark has undergone marked changes during the past 15 years.

Radical surgical procedures made possible by refined operative techniques and the advent of modern antituberculous drugs have gradually replaced the conservative treatment of earlier years: which consisted of appropriate immobilization by means of plaster casts, celluloid casts, leather braces, etc.; associated minor surgical interventions such as abscess aspiration, curettage of fistulae, sequestrotomy, etc.; and invigorating general treatment which at that time meant bed-rest, fresh air, a high calory, high vitamin, remineralizing diet, universal carbon-arc light therapy and observance of a strict daily schedule of rest in an open-air shelter, meals, afternoon rest, regulated exercise and sleep.

The introduction of radical surgery, however, has not led to any neglect of general treatment. Careful general treatment is still considered of decisive importance in this country. It is for this reason that in Denmark the treatment of extrapulmonary tuberculous conditions — not only bone and joint tuberculosis but also tuberculosis of the genito-urinary tract, lymphnodes, peritoneum and intestine — is still, and to an increasing extent, concentrated in two specialized centres.

The most important difference between the past and the present, it seems to me, is that nowadays the patients, knowing that they, like other surgical patients, have a chance to be cured in the not-too-distant future, remain psychically intact and active. Today the atmosphere in such centres is far more optimistic than only 25 years ago, when one had the impression, at times, that these patients were more or less shut off from life.

In the following pages an outline will be given of the methods of treatment used in Denmark in this small but important field.

TUBERCULOSIS OF THE SPINE

In the Hospital for Extrapulmonary Tuberculosis in Juelsminde, systematic spinal osteo-synthesis has resulted in a complete cure in about half of the patients, and a further 20 per cent have been partially restored, i. e., they can perform light work only.

The operative technique depends on the site of the disease: whether it is located in the dorsal or in the lumbar spine, *whether it is located above or below the diaphragm*. These two locations actually correspond to two forms of tuberculous spondylitis that differ clinically and pronogstically and must be treated differently:

A. *Tuberculosis in the dorsal spine* not infrequently leads to compression of the spinal cord with paresis.

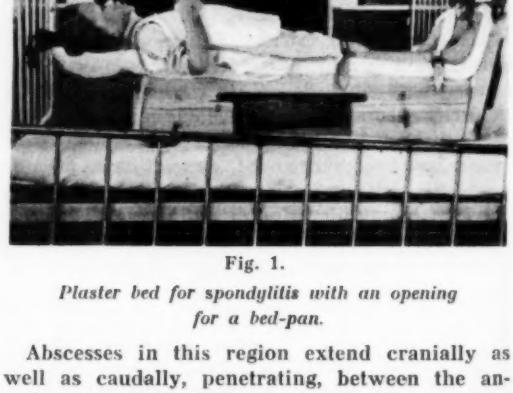

Fig. 1.

Plaster bed for spondylitis with an opening for a bed-pan.

Abscesses in this region extend cranially as well as caudally, penetrating, between the anterior longitudinal ligament and the anterior surface of the vertebrae. They penetrate into adjacent intervertebral spaces and thereby slowly produce fresh destruction, if their progression is not arrested.

The spinous processes in the dorsal region are relatively small, thin and point downward.

Surgical fusion is in this region, as a rule, done paraspinally using grafts of spongy bone. At operation one or both sulci paraspinosi are carefully skeletized, the thin layer of compacta is partly chiselled off and suitable bone grafts are flitted into the osteo-fibrous grooves thus formed.

As suggested, it is easiest to fit spongy bone,

From The Hospital for Extrapulmonary Tuberculosis, Juelsminde, Denmark. Senior Surgeon: *Hans Thomsen.*

which is readily modelled on the surroundings, and it is in this region that the large gibbosities are found.

The grafts are generally taken from the patient's iliac crest or — when operating on children — from a suitable bone donor, usually a parent.

Is goes without saying that isoplastic grafts, stored for some time in a bone bank, may also be used. But with such material resorption is occasionally observed, whereas resorption never occurs when autoplastic or fresh isoplastic grafts are used.

B. *Tuberculosis in the lumbar spine,* because of the anatomical configuration, is rarely complicated by compression of the spinal cord, and the gibbosities are usually small.

Abscesses originating in this region extend downward from the initial focus, penetrating beneath the sheath of the psoas muscle, and may eventually be palpated in the iliac fossa or distal to the ligaments.

The spinous processes in this region are strong and broad. Excellent results may be obtained by fixation with autogenous grafts taken from the patient's tibia. As mentioned, the gibbosities in this region are usually smaller than in the dorsal spine, and the grafts therefore can be almost straight. The tibial graft is fixed firmly into the gutter made by splitting the spinous processes. Further fixation of the grafts is obtained by means of metal wires which are bored through the base of the spinous processes, brought up on either side and tied over the tip of the processes. In this way a compression that promotes ossification is exercised.

The autogenous compacta grafts always become well organized, though somewhat more slowly than grafts of spongy bone.

These surgical procedures greatly benefit the patients, provided the associated abscesses are small. In case of considerable abscess formation, or when the abscesses grow markedly and perhaps cause symptoms of medullary compression, a special *abscess treatment* is indicated.

Abscesses in the dorsal region are exposed by resection of two, three or four ribs on the side where the abscess is more prominent, or — in case of asymmetric foci — where the local destruction is greater.

I use a large curved incision, the base of which follows the spine. A complete transverse division of the long muscles of the back is made, and the ribs are exposed and carefully skeletized as far dorsally as the transverse processes; with the excellent instrumentarium of S e m b, this presents no difficulties. The ligaments to the collum costae are also divided, and the pleura is loosened with a finger from the inner surface of the collum costae. The ribs are then transsected, a section of about 10 cm — counting from the capitulum — being carefully removed in the usual way.

Often pus will pour out from the point where the capituli have articulated with the spine. In that case the procedure is fairly easy; in dilating the abscess perforation carefully with a finger, a denuded corpus is felt and the extent of the abscess is determined. When the finger is withdrawn, more pus is evacuated, and the abscess cavity is carefully cleaned with a large curette and tampons.

According to the extent of the abscess, the incision is widened — possibly one or two additional ribs must be removed. (On palpation one may find necrotic areas, and these are scraped out and carefully cleaned). Large defects are filled with bone grafts — usually spongy bone taken from the patient or from a relative or, in an emergency, from a bone bank.

All of the contents of the abscess must be carefully removed. These may be of widely differing composition: thin, yellowish pus containing fibrin clots of varying size and not infrequently pea- to almond-sized sequestra, inspissated pus, putty-like masses and calcareous concretions of various sizes.

I usually use a cystoscope to make sure that the cavity is clean. After the cavity has been sprayed with penicillin and streptomycin powder, I generally close the wound by primary suture. I have seen no beneficial effect from inserting a catheter for local treatment.

If, howewer, there is no discharge of pus when the capituli costae are removed, the operation becomes technically somewhat more difficult. In these cases the pleura is freed by careful, blunt dissection with a tampon or (better) with a finger. Most often there are thread-like adhesions between the pleura and the anterior surface of the abscess. With care, however, it is usually possible to free the pleura, and the abscess is then seen and felt as a pad-like, fluctuating, flat, elongated intumescens covering the anterior surface of the diseased vertebra. Its surface is strangely smooth, and once one has palpated such an abscess one never forgets the peculiar feeling. With a Liston's forceps a blunt perforation is made at the most prominent point. This not infrequently provokes a considerable venous hemorrhage (from the transverse portions of the superior or inferior hemiazygos vein where these pass over the body of the 7th or 8th thoracic vertebra to join the azygos vein — or from ofter anastomoses between the hemiazygos and the azygos veins), which, however, usually stops after a few minutes' compression.

The abscess cavity is then cleaned and further surgical procedures are carried out as described above.

In some cases I, at least, cannot avoid tearing the pleura. Provided the tear is closed immediately (I usually do this with Spongostan —

an absorbable gelatin sponge, as sutures often tend to cut through the stiff pleura) and the lung is inflated, there are as a rule no serious consequences.

When patients with thoracic spondylitis are treated by this operation, an x-ray examination 3 to 4 months after the operation will show whether a paraspinal osteo-synthesis should be performed as well. Discrete abscess shadows may persist for a long time, but this is probably of little importance.

Abscesses in the lumbar region are incised through long oblique lumbar incisions similar to those used for exposure of the ureter. The peritoneum, ureter, etc., are gently drawn aside so that the anterior surface of the abscess becomes completely exposed. A wide incision is made. Pus, fibrin and sequestra are evacuated, and the abscess membrane is removed with sponges or tampons. After local treatment with penicillin and streptomycin the wound is sutured costotransversectomy, but sometimes, too, the results are disappointing.

When myelographic examination shows that the spinal cord is compressed by a circumscribed tuberculoma, laminectomy with removal of the intumescens may give exellent results.

A remarkable observation is that paralytic symptoms may clear up even when they have been present for a year or two. Patients with fresh pareses should always be treated conservatively for some months before surgical intervention is decided upon.

Where paralytic symptoms appear long after the spondylitic abscess has been diagnosed, evacuation of the abscess by a costotransversectomy is, however, no doubt always indicated.

Finally, to avoid any misunderstanding, it should be stressed that the patients are always placed in well-fitting plaster beds before any surgical intervention is performed; the plaster beds are mounted on a wooden frame 15 to 20 cm high, provided with a lateral opening for the bed-pan.

Further, it should be emphasized that antibiotic therapy is used only in connection with surgical interventions to protect the patients against spread of the disease during the critical post-operative period.

THE TREATMENT OF TUBERCULOUS OSTEO-ARTHRITIS IN THE HIP-JOINT

The treatment of tuberculous osteo-arthritis in the hip-joint depends on the stage of the disease when the patient comes under treatment and on the character of the disease.

The aim must be to remove the tuberculous foci as radically and as early as possible. Careful tomographic examination is of value here. Explorative arthrotomy in the hip-joint is also useful and should be performed on rather broad indications. The most difficult cases to treat rationally are those which have been given conservative, immobilizing treatment for too long; these patients develop an intense, diffuse osteoporosis that makes radiographic visualization of any circumscribed foci impossible. At operation a diffuse softening of the tissue is found, necessitating the removal of much too much viable bony tissue. Such cases must not be immobilized until the existing foci have been visualized! And this examination must be made early, before diffuse osteoporosis has developed and also before the foci have resulted in too much destruction. Such foci must be radically excised, and not infrequently the operation is so successful that the function of the joint may be partially preserved. Where the femoral head or the acetabulum has suffered too much destruc-

Fig. 2.

Resection of knee with compressing technique by means of transversing tacks and adjustable side-screws.

tion, I prefer to do a limited resection, but in that case all cartilage must be removed. It is my experience from numerous cases that bony anchylosis should be attemped (intra-articular grafts may be used), but this cannot always be achieved even with technically correct intra-articular arthrodeses.

However, once all inflammatory foci have been removed and if the joint should not — as it usually does — become painfree, the patient may be given relief later on by the addition of one or more extra-articular arthrodeses.

One may safely operate through an abscess if the patient is screened by antibiotic therapy, provided the bacilli have not become resistant through premature use of the antituberculous drugs. In such cases, one must proceed more cautiously and first bring the abscess under some measure of control by means of punctures and small incisions.

Fig. 3.

Fig. 4.

Resection of knee in a 4-year old child. The epiphyseal lines are intact.

Fig. 5.

Fig. 6.

Removal of tuberculous focus in patella + synovectomi in a 12-year old girl preserving good function.

Cases which come so late for treatment that deformities have already developed, can often be treated successfully by corrective osteotomy.

TUBERCULOSIS OF THE KNEE

Tuberculosis of the knee is always treated in adults by resection. Firmness at the site of resection can be achieved in most cases within 4 to 6 weeks if a strong compression is secured by means of transverse pins and turnbuckles. (This technique was first described in a paper from this hospital published in *Ugeskrift for Læger* in 1941).

In children the treatment must be individualized. Pea- to nut-sized subchondral foci, diagnosed by tomography, may be treated locally by curettage and the joint can thus be saved.

When the cartilagineous surfaces are worn away (note: arthrography), it is my experience that a sparing resection should be performed as long as this can be done without sacrificing the epiphyseal cartilage.

When the destructive processes have reached the epiphyseal line, deformities occur as a result of growth disturbances. Here operative treatment is best deferred until the processes show a tendency to heal under conservative orthopaedic and medical treatment. But streptomycin should only be used after careful deliberation. Save this valuable drug for the operations!

At a later stage corrective osteotomy, epiphyseodesis or a shortening operation on the contralateral extremity may be indicated.

However, the rare cases of isolated synovial tuberculosis may be treated successfully with antibiotics, but the diagnosis must be certain.

TUBERCULOSIS OF THE SHOULDER AND ELBOW

Tuberculosis of the shoulder and elbow can be treated surgically with good results by sparing resections. The cases seen in Denmark nowadays rarely show such extensive destruction that the classical resection procedures through the surgical neck are indicated.

Tuberculosis of the elbow can be resected with good functional results only if the surgeon has in layers for healing by first intention or — if the pus is very thin — around a catheter that is left in for drainage for a few days.

In patients with thoracic spondylitis and medullary compression, surprisingly good results are sometimes seen after a properly performed experience in judging how much should be resected. If he lacks this experience, a sparing resection should be made with the possibility of anchylosis. Successful anchylosis of the elbow-joint will result in a very useful upper extremity.

TUBERCULOSIS OF THE CHEST WALL

Circumscribed tuberculosis abscesses in the chest wall are no doubt generally believed to originate in the ribs or costal cartilages. Gradually, however, the view has been accepted that a good many of them arise from *suppurating tuberculous processes in the parasternal* — or in the more deepseated *mediastinal lymphnodes.*

Radical operations for these conditions should be undertaken only by a surgeon who has mastered the technique and the control of possible complications such as hemorrhage and pleural lesions.

TUBERCULOSIS OF ANKLE AND FOOT

Tuberculosis in the tarsal bones and joints should be treated surgically as soon as the local foci can be visualized. All diseased tissue should be removed and particular care must be taken not to leave any articular cartilage, the nutrition of which is compromised. As in other osteomyelitic conditions, bony cavities that have been cut out and curetted may be succesfully closed by plombage with spongy bone.

Tuberculosis of the ankle-joint in adults is best treated by resection. In this operation C h a r n l y has made systematic use of the compression principle, and this method is now being followed in Denmark. In children I have previously often used talectomy but I now prefer resection in this age-group also.

TUBERCULOSIS OF THE WRIST

In principle this condition is best treated in the same way as tuberculosis of the tarsal bones. But in long painful cases, good results may also be acheived by surgical arthrodesis. My experience is limited to arthrodesis with dorsally applied compacta grafts taken from the patient's tibia.

TREATMENT IN GENITO-URINARY TUBERCULOSIS OF THE MALE

The prime consideration must be an examination of the entire genito-urinary tract for tuberculous lesions. As is well known, renal tuberculosis is far more serious and far more chronic in the male than in the female, and this is due to the intimate connection between the male urethra and the prostate, seminal vesicles and epididymides.

Thorough urologic examination of a male patient requires: urography, cystography, vesiculography, urethrography as well as examination of bladder urine, urine from the left and right kidney and voided urine. In this hospital cultures are always made, and the type of the bacilli and their resistance to the commonly used antibiotics are determined.

Cystoscopic and urethroscopic examinations are carried out under pethidin analgesia — as described in a paper from the Finsen Institute (G a m m e l t o f t & al. 1953).

In Denmark we have begun, with great expectations, to carry out partial nephrectomy, a. m. S e m b, and thus far at least the results have been entirely satisfactory.

Fig. 7.

Fig. 8.

Urography before and after renal resection on the left side.

A. Cases of uni- or bilateral renal tuberculous bacilluria with no radiographic changes and no microscopic formed elements in the urine.

These should not be treated with antibiotics, as most of them tend to heal spontaneously — and to risk the emergence of streptomycin-resistant strains is in my opinion unjustifiable. A careful follow-up is indicated, including frequent microscopic examinations of the urine and uropyelography every 3 to 4 months.

Other surgeons may hold a different opinion. The management of these cases is a matter of temperament and cannot as yet be determined objectively.

B. Cases of uni- or bilateral renal tuberculous bacilluria with no radiographic changes but with recurrent microscopic hematuria and pyuria (by definition these are always quite moderate).

These cases reflect a transition from cortical to medullary, destructive renal tuberculosis. Combined treatment with streptomycin and p-aminosalicylic acid (PAS) is indicated. In this group, too, careful observation is required.

C. Cases of renal tuberculous bacilluria with a large amount of formed elements in the urine and with slight radiographic changes.

Groups B and C cannot be clearly separated as the more subtle radiographic changes such as ragged fornix contours, recess formation, papillary ulceration, etc., are often so uncertain that the classification may be made on a more or less well-founded estimate. The treatment will therefore be the same for B and C: administration of streptomycin and PAS, and follow-up.

D. Cases of renal tuberculous bacilluria with small but definite radiographic changes, i. e., up to pea-sized contrast shadows in the renal parenchyma.

Here medical treatment with streptomycin and PAS should be tried — under close supervision. The treatment must be continued for at least 4 to 6 months. There is a considerable risk of development of resistance to streptomycin, and if at the end of this period the urine still contains tubercle bacilli and other pathologic formed elements, and if the destructive processes are confined to one of the three segments of the kidney, it is no doubt best to perform a resection. Some specialists recommend a longer period of medical treatment, and it must be admitted that calcification or encapsulation of the small cavities may be observed, even in long-standing cases. Close follow-up is required.

E. Fairly large, unilateral, cavernous lesions localized to one renal segment (hazelnut- to walnut-sized cavities.

Treatment: Partial nephrectomy with pre- and post-operative chemotherapy.

F. Fairly extensive, unilateral, destructive disease involving the major part of one kidney with healthy contralateral kidney (including unilateral pyonephrosis or putty kidney).

Treatment: Nephrectomy with pre- and post-operative chemotherapy.

G. Large cavernous lesions in one kidney and minor changes in the other.

Treatment: Nephrectomy plus prolonged, intermittent chemotherapy.

H. Moderate destructive lesions in both kidneys.

These cases are first subjected to prolonged — possibly intermittent — chemotherapy. The response to chemotherapy will, as a rule, permit evaluation of the case. There may be regression of the tuberculous processes in both kidneys, and it may also happen that the disease in one kidney progresses, the cavities enlarging. The treatment will be determined accordingly. Uni- or bilateral resection may become indicated.

I. Extensive cavernous disease in both kidneys.

Prolonged, intermittent treatment with streptomycin. If one kidney shows improvement, removal of the other kidney may become indica-

ted. Should the disease in the remaining kidney become arrested, an appropriate resection can then be carried out.

K. Complete destruction of one kidney — with pyonephrosis or putty kidney — and destructive changes localized to one segment in the other.

Nephrectomy — intensive chemotherapy — later possibly resection of the remaining kidney.

Male genital tuberculosis can largely be regarded as a symptom of renal tuberculosis. Yet probably 20—30 per cent of all cases of tuberculous epididymitis are of hematogenous origin. At any rate, 50 per cent of the patients with tuberculosis epididymitis have in addition renal tuberculosis.

Orchidectomy should not be performed unless the circumstances are quite exceptional. With a good technique, removal of the epididymis will practically always be sufficient. Many surgeons are unduly alarmed by the more or less extensive abscess which nearly always has developed between the epididymis and the orchis. But such an abscess constitutes absolutely no indication for a simultaneous removal of the orchis.

Tuberculosis of the prostate is easily diagnosed by urethrography with a suitable contrast medium (Umbradil viscous — ASTRA). If a more fluid contrast medium is used, the prostatic destructions are often overlooked.

It is my experience that these prostatic lesions, even though they give rise to long-lasting tuberculous bacilluria, run a relatively benign course. On careful follow-up by repeated urethroscopic examination, it is seen that the sharply demarcated cavity openings gradually become enveloped by cicatrizing, shrinking tissue. Presumably this process may be accelerated by electrocoagulation.

FEMALE GENITAL TUBERCULOSIS

It is difficult to give a brief description of the principles of treatment. In many cases the diagnosis may be obtained by culture of the cervical secretion, an examination which apparently is often neglected and which perhaps is not yet very well-known.

Circumscribed, movable masses should be treated by radical surgery. In the more acute cases it is best to refrain from surgical intervention, at any rate until the patient has been given 4—5 weeks' intensive antibiotic treatment. The *à chaud* operations that formerly were so frequently performed on patients presenting acute abdominal symptoms resulted far too often in serious intestinal fistulae.

Isolated endometrial tuberculosis. Here I have obtained excellent results with abrasion of the uterine mucosa complemented by streptomycin treatment. The abrasion is repeated at monthly intervals. In many of the cases thus treated, the mucosa which at first presented the microscopic changes typical for tuberculosis will, at subsequent microscopic examinations, show endometritis with a few granulomata — simple endometritis — and finally a return to normal.

Most of these cases are diagnosed on curettage in patients referred to a gynaecologic department because of sterility.

More deep-seated endometrial tuberculosis often requires radical surgical treatment.

TUBERCULOSIS OF THE LYMPH NODES

The diagnosis must be certain. If the affected lymph nodes are accessible to surgical therapy, radical procedures are indicated as the condition is less benign than it has previously been assumed.

In the great majority of cases suppurating cervical lymph nodes in children and adolescents must pathogenetically be regarded as components of a primary complex originating from a primary lesion in the tonsils.

Most cases of tuberculous mediastinal lymphadenitis are still treated conservatively. It is not known, however, how much damage tuberculous mediastinal lymph nodes may do by causing hematogenous or canalicular dissemination at some time or other, as the processes that take place in the chest cannot be seen and most often can "only" be diagnosed clinically. But there is no reason to doubt that tuberculous lymph nodes in the thorax and mediastinum may be the site of extensive destructive processes that are in every respect analogous to those that can be observed — even by laymen — in the cervical region.

Tuberculosis of the mesenteric lymph nodes begins as part of the primary complexes originating in the intestinal tract. It may give rise to suppuration, circumscribed or diffuse peritonitis, adhesions, etc.

The above-mentioned forms of tuberculous lymphadenitis always leave calcified residues which it must be presumed will be demonstrable by x-ray for the remainder of the patient's life.

We, therefore, subject every patient with extrapulmonary tuberculosis to systematic radiographic examination of the cervical region, mediastinum and abdomen. Exposures should be made with hard as well as soft rays so that no lesions are overlooked. Occasionally monstrous calcifications are observed in a large number of the lymph nodes which drain the organs of entry.

COMMENTS

Less than 20 to 30 years ago, extrapulmonary tuberculosis in Denmark was often due to bovine tubercle bacilli. In 1947, 25 per cent of a series of cases from this hospital were of bovine origin, whereas today bovine tubercle bacilli can be isolated in only 1 per cent of the cases. From a clinical point of view there is no difference between cases due to bovine or to human tubercle bacilli.

It should be emphasized that in principle we do not use streptomycin and other antituberculous drugs for independent treatment of extrapulmonary tuberculosis but reserve these drugs for pre- and post-operative chemotherapy to provide "coverage" for patients undergoing surgery. We consider radical surgical treatment so important that we dare not risk the development of drug resistance before the patients are ready for surgery.

Immobilizing treatment is used in connection with operations on the extremities and the spine, but only exceptionally as an independent treatment.

We also hold that the use of spinal braces after rational surgical treatment of spondylitis is in the great majority of cases superfluous and may even be harmful — not only to the muscles of the back but also to the patient's psyche.

Universal carbon-arc light therapy has practically been abandoned in this country. In our opinion it has never been shown that this form of therapy has any real effect on extrapulmonary tuberculous disease. We do not object to light therapy as a means of improving the patient's general condition, but we do not consider it any more important than open-air treatment, a well-balanced, high-vitamin, remineralizing diet, etc.

Finally a few words about the prevailing view in this country of the rôle of traumata: It is increasingly held that well-defined trauma in practise play no rôle in the localization of extrapulmonary tuberculous disease, and it is even questioned whether well-defined acute traumata commonly have any greater effect on already established tuberculous lesions in the bones, joints, kidneys, abdominal region or epididymis.

As far as we know, about 200—300 persons develop extrapulmonary tuberculosis each year in Denmark, and there are in all about 2000—3000 patients with active disease or residual disabilities. There has been a large and constant decrease in the morbidity from pulmonary tuberculosis, so no doubt a decrease in the number of extrapulmonary cases will follow. But as is well known, the latter "trail" well behind the pulmonary cases, and the end of the road is not yet in sight.

Generally speaking, the factors of greatest prophylactic value have no doubt been:

1) eradication of tuberculosis in cattle.
2) improved hygienic conditions.
3) early detection of source cases through the numerous tuberculosis dispensaries.
4) better living conditions with respect to housing as well as nutrition.
5) increased use of BCG-vaccination (?).

It is, however, hardly possible to point to any measures as being particularly effective, as the incidence of tuberculosis in Denmark for many years has shown a steady decrease.

As a Norwegian colleague — Thrap-Meyer — so aptly puts it — "Tuberculosis is burning out".

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TEACHING AND CHECKING OF INTERPRETERS OF FLUOROGRAMS WITH A NEW PHANTOM IMITATING LUNG-INFILTRATES

By HELGE NIELSEN and KAJ-W. NOSCHIS

The teaching of the reading of fluorograms and the checking of interpreters are intricate affairs and constitute some of the more important links in the chain of still unsolved problems in the photofluorographic process.

Several difficulties are met with when the teaching has to rely on fluorograms taken during the daily work at a Tuberculosis Clinic and when the trainee is first shown those shadows in the fluorograms which need a roentgenogram as a check, and is then allowed to find those contrasts himself; first under constant and zealous supervision, later alone when at long last he is considered an "experienced" but now unchecked interpreter of fluorograms.

The teaching is met with difficulties because pathologic findings will not be frequent in fluorograms from the daily routine, and still less frequently will these fluorograms be suitable for demonstrating those vague and indefinite shadows which are caused by incipient pathologic conditions.

During the reading it may not always be possible for the instructor to point out with sufficient conviction the subtle differences between the "suspicious" shadows caused by small pathologic changes, and the no less "suspicious" increases of markings, which are solely found in the flourograms and which cause the notorious overreading.

From the Tuberculosis Clinic, Copenhagen.
Chief: *Knud Winge.*
Department for Mass Examinations.
Deputy Chief: *Helge Nielsen.*

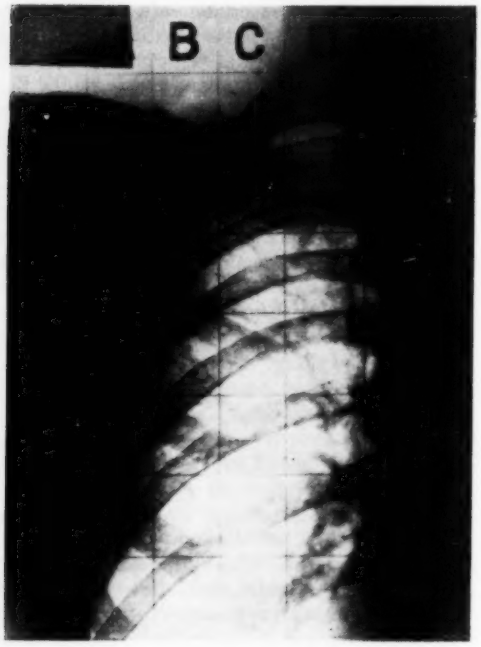

Fig. 1-a.

For teaching purposes a normal chest is fluorographed through a plate onto which is fixed an image giving graph of reference.

That uncertainty is often increased, because several days will pass before the full-sized roentgenogram has been taken as a check, and during that time the trainee forgets everything about the corresponding contrast. Of course a re-reading of the fluorogram is possible, but as there are no possibilities of exactness in localization, that procedure is seldom more than a biased guess.

The checking of interpreters of fluorograms is hampered by the fact that there is no satisfactory solution of the problems connected with the identification of those fluorograms on which there are shadows at least to be discovered by the reader, not to mention the problem of correct interpretation of the shadows discovered.

Because of the above — mentioned difficulties we have tried to create an appropriate material of fluorograms by means of phantoms (fake-infiltrates).

First we used "optical" fake-infiltrates which were placed inside the optical part of the photofluorographic installation and consisted of a positive copy of a normal chest and of positive copies of lung infiltrates found in roentgenograms of patients with infiltrates of appropriate size and density. The manufacture of the components was very difficult and the utilization was hampered by the fact that both components had to be placed inside the optical system.

As a variation the fake-infiltrates are not copies but are substantial and therefore able to give a roentgen image on the fluorescent screen with the same contrasts as normal lung infiltrates. Such fake-infiltrates are not too difficult to make and it is possible, by means of visual comparison and densitometri, to let the fake-infiltrates imitate the contrasts of ordinary infiltrates of convenient size and density. At last, we reached the procedure where the other component of the phantom was also made substantial by using the normal human chest as background. Fluorograms showing pathologic shadows are now made by fluorographing a normal chest through an imagegiving graph of reference fixed on a plate onto which the fake-infiltrates are attached.

By means of that procedure it is easy to create a huge variation in the fluorograms and it is possible to meet demands motivated by differences in the aptness of the traines, and in the pathological findings in various countries.

It is also possible by means of copying to ensure uniform teaching and checking within greater organizations, thus enabling a correction of that part of the variation in morbidity figures which is caused by differences in the photofluorographic technique used and in the skill of the interpreters.

A series of fluorograms for teaching purposes consists of three pictures. The *first* is a fluoro-

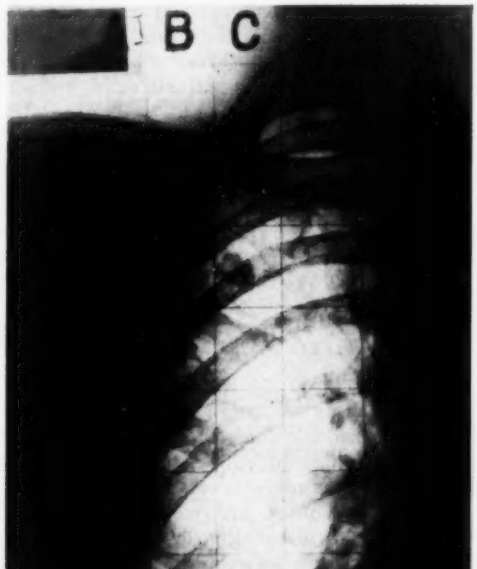

Fig. 1-b.

The same normal chest as in Fig. 1-a is fluorographed through the same image — giving graph of reference fixed on the plate onto which are attached two fake-infiltrates (No. 17 and 18), one in square C-2 (right first intercostalspace) and one in square B-3 (right second intercostalspace).

Fig. 1-c.

After each "abnormal" fluorogram with fake-infiltrates an additional picture is taken of the two fake-infiltrates still attached to the plate with the graph of reference giving the correct and complete interpretation of the "abnormal" fluorogram.

gram of a normal chest taken through the plate on which the graph of reference is fixed (Fig. 1-a), the *second* is the same chest fluorographed — in a projection as similar as possible to that used in the first picture — through the plate onto which is now also attached fake-infiltrates of the desired densities and in an appropriate number and localization (Fig. 1-b). Finally the *third* picture is of the fake-infiltrates still attached to the plate but now without a superimposed chest (Fig. 1-c).

In the initial phase of the teaching the trainee has exclusively to learn how the fake-infiltrates — and accordingly the real infiltrates as well — look in a fluorogram, and he must avoid, as much as possible, picking up irrelevant contrasts. The third picture in the series gives at once the exact localization of the fake-infiltrates, and by means of the system of reference it is possible for him to locate with accuracy the corresponding parts of the lungs on the first and second fluorogram. A direct comparison of the relevant regions will disclose a difference in transparency and opacity (density), and as that difference is entirely due to the fake-infiltrate, the difference will tell the reader how a natural infiltrate looks in a fluorogram.

During the next phase the trainee tries to locate the fake-infiltrate on the second picture without first consulting the "solution" given by the third picture. That is done by systematically scanning the lung fields with his central vision constantly comparing corresponding regions on the two fluorograms.

In this phase the trainee builds up — partly unconsciously — a mental image of a fluorogram of an average, normal human chest, and little by little he acquires the capability of reacting whenever his central vision registers something additional superimposed onto that mental normal fluorogram.

After some time he does not even need the systematic comparison with the first picture because he is now able to rely entirely upon his mental image during the scanning of the abnormal fluorogram. Soon he is relying on his peripheral vision as well, and is now at long last in the final phase of learning as a trainee, i. e., the phase of concentration, detection and scrutiny, but unfortunately also of assessing.

In order to be able to demonstrate for the trainee how fake-infiltrates look on roentgenograms, such pictures have been taken of the same chest with and without fake-infiltrates superimposed.

It has to be pointed out, however, that because the fake-infiltrates are placed near the fluorescent screen the contrasts of the image will not be influenced by secondary radiation, and there will be no unsharpness caused by movements because the fake-infiltrates do not move during the exposure; neither will there be unsharpness caused by the size of the anode. The first objection is perhaps not valid because of the use of a grid in photofluorography, and the second and third factor have been compensated by the imitation of an infiltrate moving in a certain distance from the x-ray film.

But in the fluorograms the fake-infiltrates will not be given the same magnification as ordinary infiltrates, and therefore the trainee is, in fact, disclosing infiltrates which are smaller than those on the corresponding roentgenograms, but perhaps he is helped by an increased gradient of contrast.

The trainee should not participate in the reading of fluorograms taken during the daily routine at a Tuberculosis Clinic until he is able to detect the infiltrates by means of his peripheral vision and his mental image of a normal fluorogram.

At the beginning he is, of course, not able to read without constant supervision and help from a more experienced interpreter, because such fluorograms contain many types of pathologic shadows which the trainee has had no opportunity of meeting during the preliminary teaching and training.

It is possible to control the progress of the trainee and to check the efficacy of more experienced interpreters by means of film-strips consisting of an appropriate number of normal and abnormal fluorograms made in the same way as those for teaching purposes.

Or, it can be done as in the town of *Uppsala*, in Sweden, where through the impetus of W e g e l i u s we were able to make a check-film consist-

ing of 101 fluorograms of the size 53×53 mm. In that town two photofluorographic units were working and it was therefore possible to use one of the apparatus to that end. The board with the graph of reference was mounted on that unit and in a certain number of cases one or two fake-infiltrates as well. In *Copenhagen* we read the film in order to determine how often and on which fluorograms the fake-infiltrates actually were situated "in the lung fields", because only those pictures had to be identified by the readers in an experiment carried out at the "Mass Radiography Centre of the Royal Swedish Medical Board" in *Stockholm*.

The analysis of the material gained in that experiment is not finished, but as a preliminary result it can be stated that it is of paramount importance to check the deleterious influence of the human factor, one of the links in the chain of still unsolved problems in the photofluorographic process.

SUMMARY

A procedure is described which is helpful in the teaching of interpretation of fluorograms and in the checking of interpreters, through the use of phantoms (fake-infiltrates) which imitate small lung-infiltrates in form, structure and density.

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ON THE MORPHOLOGICAL SEX DIFFERENCE IN NEUTROPHILIC AND EOSINOPHILIC GRANULOCYTES

By POVL RIIS

In several reports published since 1949 Barr et al. have related a morphological sex difference in the nerve cell nucleus of various mammals, including man. (1, 2, 6).

In 1953 Moore, Graham and Barr (7) demonstrated an unquestionable morphological difference in the content of chromatin of cutaneous cells between males and females.

Sex identification of teratomatous cells and cancer cells has been reported (5, 8).

In 1954 Davidson and Robertson Smith (4) reported that similar morphological sex differences had been observed in human neutrophilic granulocytes. A special feature of female neutrophilic granulocytes was the appearance of a characteristic stalky nuclear appendage. The frequency of such sex manifestation varied from 1:16 to 1:98, or on an average 1:38. On reviewing an extensive number of sections, the authors came to the conclusion that the sex manifestation reported was most frequent in shifts to the right, whereas the incidence diminished in shifts to the left and was rare in non-segmented nuclei. No examination was made of the correlation between the degree of segmentation and the imprint of sex.

No mention was made of the occurrence of the phenomenon in eosinophilic cells.

MATERIAL

A material comprising 15000 granulocytes was studied very closely by means of standard microscopy (low power m.; power of magnification approximately 150 times) and by high power magnification (approximately 1500 times) by means of immersion objective. These 15000 cells represent 500 cells studied in 16 women and 14 men — the series comprises predominantly normal individuals. The sections used were Giemsa-stained smears, prepared as for differential count.

A high quality of the preparations used, more particularly of stain, is necessary to obtain good specimens.

The origin of twenty-five of the preparations was unknown to the author previous to the study. Sex identification was possible in all cases on the basis of the microscopic study. The probability of having correctly established sex identification in twenty-five cases *by chance* is diminutive — i. e., 1:5200000. — which bears witness to the fact that the phenomenon observed is subject to regularity.

The morphological characteristics encountered were as follows:

1) "Drumsticks" (Fig. 1). Approximately 1,5 μ sized, stalky nuclear appendages, rich chromatin.

These are only met with in the granulocytes of females, and the incidence in the present study varies from 1:13 to 1:100, or on an average 1:29.

Among 8000 granulocytes of females a total of seven "drumsticks" were encountered in eosinophilic cells.

A close study of the nuclear outline of basophilic granulocytes was not possible owing to the presence of the coarse intensely staining granules.

No morphological sex differences were seen in the nuclei of lymphocytes and monocytes between males and females.

From the Copenhagen County Hospital, Medical Department F. Head: *F. Wulff.*

Fig. 1.
Centrally placed neutrophilic granulocyte with typical "drumstick" arising from right aspect of the nucleus.

As to the relation between the incidence of "drumsticks" and the number of nuclear segments — see Table I.

2) "Rackets" (Fig. 2). Approximately 1,5 μ sized stalky nuclear appendages, poor in chromatin. The appendage has a light coloured centre as distinguished from the intensely stained nuclear mass of "drumsticks". "Rackets" are only seldom met with in males and are never seen in females.

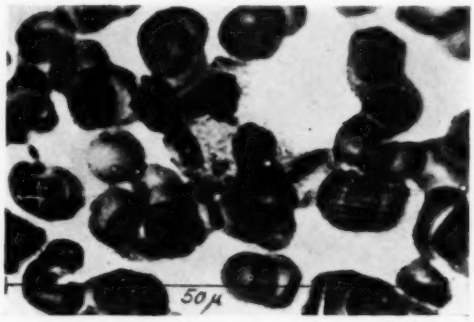

Fig. 2.
Centrally placed neutrophilic granulocyte with "racket" arising from the nuclear segment to the right.

Among the 7000 neutrophilic male granulocytes included in this study eight "rackets" were encountered, i. e., 1:875. Six out of the eight "rackets" wer found in cells with three nuclear segments. (Table I).

3) "Small clubs" (Fig. 3). In both males and females the so-called "small clubs" were present. The nucleus of these is less than 1 μ and is only rarely seen in the above — mentioned standard microscopy. They are far more frequent in males than in females and to an experienced investigator

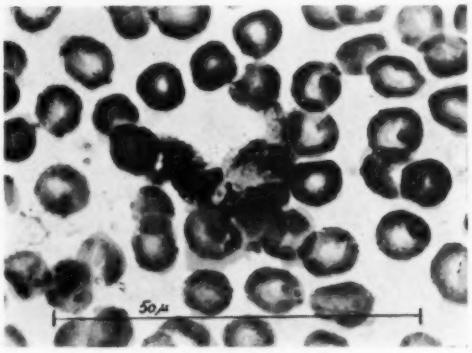

Fig. 3.
Centrally placed neutrophilic granulocyte. In lower nuclear segment of the left is seen a centrally orientated "small club".

are never confused with "drumsticks" and "rackets". In Table I is stated the relation between incidence and degree of segmentation. The total number stated represents a minimum value, smaller nuclear processes, not possesing the characteristic structure seen in Fig. 3, not being included in the material.

4) Sessile, nuclear processes, rich in chromatin, of an order of 1—2 μ. Most frequent in females. They may perhaps be conceived as a varied morphological manifestation of the sex chromatin, but they are not well-defined and are debatable. As a consequence they are left out of consider-

Table 1.

Number of nuclear segments.		1	2	3	4	5	≧ 6
"Drumsticks"	Neutrophilic granulocytes.	(35) 13%	(71) 27%	(95) 36%	(51) 20%	(8) 3%	(2) 1%
	Eosinophilic granulocytes.		5	2			
"Rackets" in neutrophilic granulocytes				6	1		1
"Small clubs" in neutrophilic granulocytes		(5) 6%	(29) 36%	(34) 43%	(12) 15%		
Number of nuclear segments in terms of percentage of a normal material.*)		2,84 ±2,79	22,04 ±6,34	54,28 ±5,31	18,06 ±6,89	2,78 ±2,10	

*) A study has been made of fifty individuals comprising 5000 neutrophilic granulocytes. The control material derives from W. M. Davidson et al.: "The Pelger-Huët Anomaly." (3).

ation as a criterion for the sex identification of granulocytes.

A single source of error must be mentioned. In standard microscopy, 2—3 μ sized nuclear segments may be confused with "drumsticks". However, a close study by high power microscopy will reveal the dual anchoring of the nuclear segment by strands to adjacent segments (Fig. 4), as distinguished from the anchorage by a single strand of a "drumstick-process". An end-placed nuclear segment, rich in chromatin, of an order of 2 μ is not met with in the granulocytes of males.

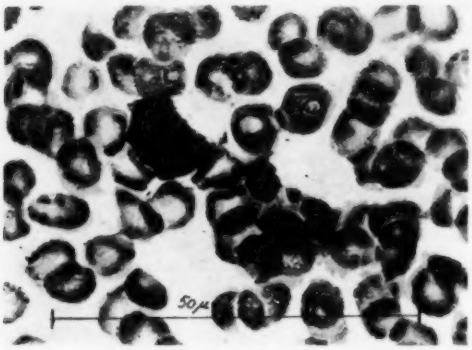

Fig. 4.
To the right is seen a neutrophilic granulocyte with a small intermediary nuclear segment.

DISCUSSION

The above-mentioned method of sex identification of granulocytes in man must be considered absolutely reliable.

Conclusive evidence has been established by the present study that the characteristic "drumsticks" are encountered in both neutrophilic and eosinophilic granulocytes.

From Table I it appears that the greatest frequency of "drumsticks" is not met with in the strongly segmented nuclei. On the contrary, among a greater number of granulocytes from normal individuals, the greatest number of "drumsticks" — in relation to the number of nuclear segments — were found to the left of the maximal degree of segmentation.

According to Barr et al., Davidson and Robertson Smith, the reported differences in nuclear morphology may be conceived as being a product of the chromatin-rich xx chromosome complement of female cells. In the absence of direct evidence it has been suggested that the "drumstick" process reported is a direct manifestation of the xx chromatin.

A female patient suffering from chronic myelogenous leukemia is included in the present study. A single immature granulocyte was influenced (Fig. 5). A close study of leukemia cells with special reference to the nature of sex chromatin will be desirable.

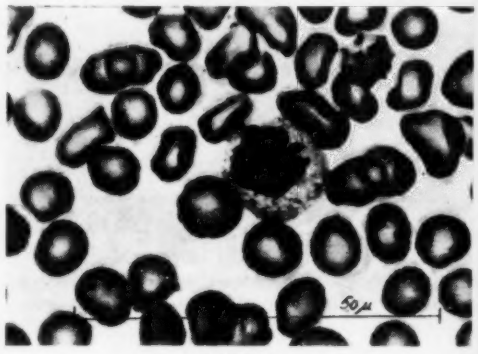

Fig. 5.
Leucocyte from patient suffering from chronic myelogenous leukemia. Upwards to the right in an indent of the nucleus a "drumstick" is seen.

Apart from the theoretical aspect of the problem, the reported morphological sex differences in the nuclei of granulocytes, depicted in this paper, will be of interest in determining the complement of sex chromosomes in hermaphrodites, and may in certain cases be made available for purposes of forensic medicine.

SUMMARY

The method of Davidson and Robertson Smith in determining the complement of sex chromosomes in granulocytes of man, on the basis of certain morphological characteristics, has proved valid. The characteristic nuclear appendages are being described. In the present material the frequency of these nuclear appendages is highest in granulocytes having two or three nuclear segments. The theoretical and practical aspect of the phenomenon is briefly reviewed.

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